Newborn Screening Guide

Newborn Screening Guide

Revised 12/15/05

Important News on Expanded Newborn Screening

As most of you are aware, SB 24 was passed in the 2005 Legislative Session to expand the number of conditions for which newborn screening is completed in Kentucky. The complete expansion will be effective December 31, 2005, and at that time a total of 29 conditions will be included on the screen which puts Kentucky in line with the national recommendation from the March of Dimes. Changes began in the newborn screening process effective July 2005 and the bullets below highlight important information for submitters of newborn screens and hospitals.

For All Submitters of Newborn Screens, including Hospitals:

- The new technology will detect disorders at 24 hours of age. The optimal specimen should be collected at 24 hours of age, but no later than 48 hours of age.
- If the infant is going to receive a blood transfusion, if possible, get the blood spot specimen prior to giving the transfusion even if the infant is not 24 hours of age.
- Antibiotics need to be documented on the filter paper card but will not automatically require a repeat.
- Demographic information and physician of record should be verified with the parent on the specimen to ensure that the physician and family can be contacted quickly in the situation of a positive screen.
- The specimen needs to be mailed to the state lab within 24 hours of collection, so the mail process at the submitting facility should examine their mailing procedure to assure entry into the USPS (United States Postal Service) as soon as possible after collection.
- There will be an educational presentation available on https://ky.train.org

Specific to Hospitals:

- Hospitals are required to have a newborn screening coordinator designated with the Department for Public Health Newborn Screening Program on an annual basis in January. Newborn Nursery nurse managers will be contacted to provide information.
- Hospitals will be required to implement a protocol to assure all newborns receive a newborn screening blood test and submit to the Department for Public Health.
- Hospitals will also be required to provide educational information to parents regarding newborn screening. This information is available on the HRSA website http://mchb.hrsa.gov/programs/default.htm and scroll down to Newborn Screening brochure.

Follow-Up:

Short Term follow-up for abnormal or unsatisfactory specimens is conducted by state staff at the Department for Public Health.

Abnormal Result

- The state lab notifies the follow-up staff of the abnormal result.
- The follow-up staff contacts the primary care physician listed on the NBS filter paper card by telephone with further action and faxes information to their office.
- The Department for Public Health contracts with University of Kentucky and the University of Louisville for specialty clinic referrals.

Unsatisfactory Specimen

- The laboratory staff mails out results either with a letter explaining to repeat only one test or if no letter is attached, the entire specimen needs to be repeated.
- If a repeat specimen is not received within 10 days, a letter is mailed to the parent explaining that no repeat has been received and to contact their baby's PCP.

After analyzing the data on the T4 levels the new cut off value will be 5.0ug/dL effective December 5, 2005. We will continue to monitor this and may adjust further in the future.

Disorders included in the screen as of December 31, 2005 are:

Disorders of Amino Acid Metabolism:

1. Phenylketonuria (PKU)
2. Maple Syrup Urine Disease (MSUD)
3. Homocystinuria (HCY)
4. Citrullinemia (CIT)
5. Arginosuccinic acidemia (ASA)
6. Tyrosinemia type 1 (TYR 1)

Disorders of Fatty Acid Oxidation

7. Medium chain acyl-CoA dehydrogenase deficiency (MCAD)
8. Very long chain acyl-CoA dehydrogenase deficiency (VLCAD)
9. Long-chain hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)
10. Short-chain acyl-CoA dehydrogenase deficiency (SCAD)
11. Trifunctional protein deficiency (TFP)
12. Carnitine uptake defect (CUD)

Disorders of Organic Acid Metabolism

13. Isovaleric acidemia (IVA)
14. Glutaric acidemia type 1 (GA 1)
15. 3-hydroxy-3-methyl glutaric aciduria (HMG)
16. Multiple carboxylase deficiency (MCD)
17. Methylmalonic acidemia (Cbl A, B)
18. Methylmalonic acidemia mutase deficiency (MUT)
19. Propionic Acidemia (PA)
20. β-ketothiolase deficiency (BKT)
21. 3-Methylcrotonyl-CoA carboxylase deficiency

Hemoglobinopathies

22. Sickle Cell Disease
23. Hemoglobin SC Disease
24. Hemoglobin S/β-thalassemia

Others

25. Galactosemia
26. Biotinidase deficiency
27. Congenital Adrenal Hyperplasia (CAH)
28. Cystic Fibrosis (CF)
29. Congenital Hypothyroidism (CH)

For more information contact Sandy Fawbush at 502-564-3756 Ext 3761 or sandy.fawbush@ky.gov

Insert copy of your hospital protocol and submit a copy of protocol and the complete the contact information sheet for the Newborn Screening Coordinator at your facility and mail to:

Department for Public Health
Newborn Screening Program
275 East Main St HS 2GW-C
Frankfort, KY 40621

Newborn Screening Coordinator Information

Facility Name _____

Coordinator Name _____

Telephone Number _____

Email _____

Completed by:

_____ _____
Name Title

Please complete and fax to the Newborn Screening Program 502-564-1510.

PROPER SPECIMEN COLLECTION PROCEDURE

The filter paper forms should be stored in a cool, dry place. Be sure to take note of the form expiration date printed on the filter paper margin below the circles. The filter paper forms are to be used on or before the expiration date. Destroy all outdated forms immediately and request a new supply from the Kentucky Public Health Laboratory. Order no more forms than can be used in 6 months.

Gloves should be worn for personal safety. Care should be taken to avoid contamination of blood collection circles with antiseptic solutions, powders, lotions or other materials, which may adversely affect the testing process.

1. When collecting blood, fold back the cover sheet to expose the filter paper. Do not touch or handle the filter paper before or after applying blood.

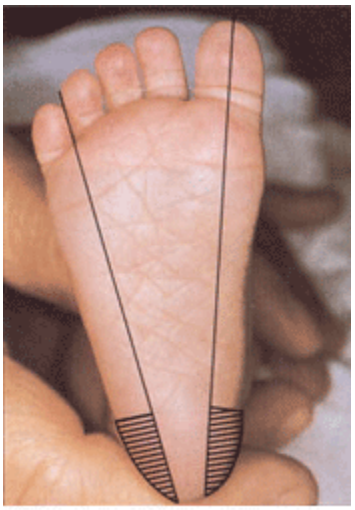
2. Position the infant with feet lowered below the heart to help to increase the blood flow.

3. Warm the heel to increase the blood flow to the area by covering the puncture site for three to five minutes with a warm, moist towel which has been run under tap water at a temperature of not more than 42 degrees centigrade or 107.6 degrees F.

4. Clean the puncture site with a sterile alcohol pad. Allow to air dry. Excess alcohol may cause hemolysis and denature some of the enzymes tested.

5. Use a sterile disposable lancet with a 2.0 mm tip or an automatic lancet to perform a swift clean puncture in the areas indicated on the diagram. Wipe away the first drop of blood with dry sterile gauze.

   Recommendation for Heel Puncture Site in Newborns:
   Perform punctures on the most lateral portions of the plantar surface (in the hatched portion of the foot in the photo to the right).



Hatched area (▨) indicates safe areas for puncture site.

6. Allow a large drop of blood to form. To enhance blood flow during collection, very gentle intermittent pressure may be applied to the area surrounding the puncture site. Excessive "milking" causes an admixture of tissue fluids with the blood specimen, resulting in an unsatisfactory specimen.

7. Do not use a capillary tube. Lightly touch the filter paper against a large drop of blood and allow a sufficient quantity of blood to soak through to completely fill the circle. Apply blood to one side of the filter paper only, allowing full saturation of each circle area. Either side may be chosen for this procedure. Fill all circle areas. Do not layer successive small drops of blood to the same circle. Avoid touching or smearing the blood spots.

8. If blood flow is diminished, repeat steps three through six with sterile equipment.

9. Special Considerations: Do not draw from intravenous lines where TPN or blood is being infused. For other types of IV fluids, make sure the line has been thoroughly flushed before attempting specimen collection. Avoid syringes with additives. Draw 2 to 2.5 cc from the line before sample is obtained. Spot the card immediately after specimen collection.

10. Allow the blood specimens to air-dry for at least 3 hours on a flat, nonabsorbent surface protected from heat or direct sunlight. Do not refrigerate the samples.

11. Ship collection forms to the Kentucky Public Health Laboratory after at least 3 hours drying time. Remember to **"Draw, Dry, and Drop (in the mail)."** Do not accumulate or "batch" specimens before shipping since this may result in specimens too old to test. When placing more than one specimen in an envelope, alternate orientation of collection forms so that blood spots on adjacent forms are not in contact. Delayed submission to the laboratory may result in significant delay in identification of an infant with a disorder.

12. After completing the form and collecting the specimen, ship to: Department for Public Health, Division of Laboratory Services, P. O. Box 2010, Frankfort, KY 40602.

The Kentucky Public Health Laboratory assumes responsibility for testing only; whoever submits specimens must assume liability for proper identification, collection and prompt delivery of specimens to the State Lab.

Neonatal Screening Blood Specimen Collection and Handling Procedure

1

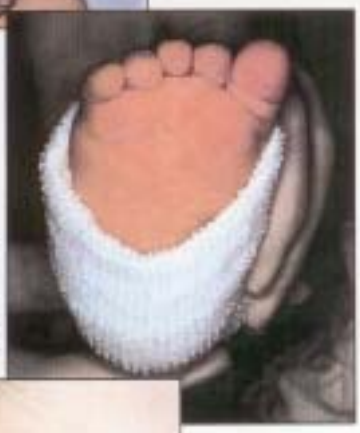
Equipment: Sterile lancet with tip approximately 2.0 mm, sterile alcohol prep, sterile gauze pads, soft cloth, blood form, gloves.

2

Complete ALL information. Do not contaminate filter paper circles by allowing the circles to come in contact with spillage or by touching before or after blood collection. Keep "SUBMITTER COPY" if applicable.

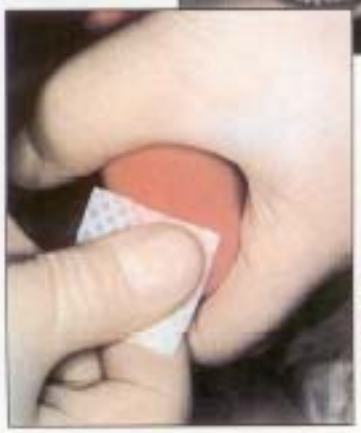
3

Hatched area ( ) indicates safe areas for puncture site.



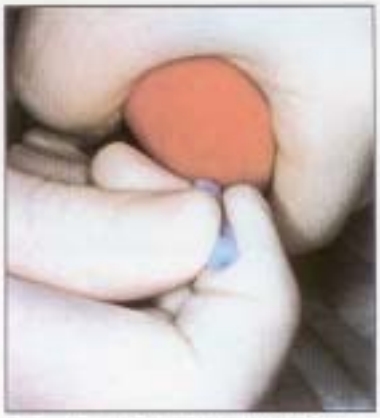
4

Warm site with soft cloth, moistened with warm water up to 41°C, for three to five minutes.



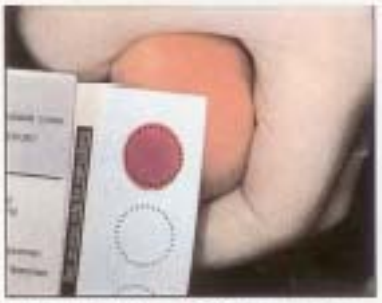
5

Cleanse site with alcohol prep. Wipe DRY with sterile gauze pad.



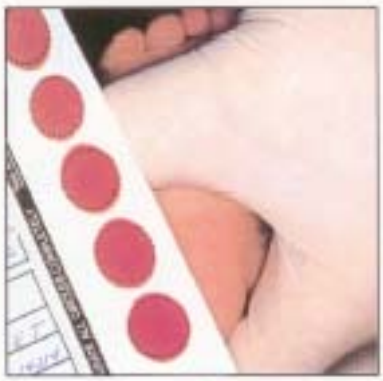
6

Puncture heel. Wipe away first blood drop with sterile gauze pad. Allow another LARGE blood drop to form.



7

Lightly touch filter paper to LARGE blood drop. Allow blood to soak through and completely fill circle with SINGLE application to LARGE blood drop. (To enhance blood flow, VERY GENTLE intermittent pressure may be applied to area surrounding puncture site.) Apply blood to one side of filter paper only.



8

Fill remaining circles in same manner as step 7, with successive blood drops. If blood flow is diminished, repeat steps 5 through 7. Care of skin puncture site should be consistent with your institution's procedures.

9

Dry blood spots on a dry, clean, flat, non-absorbent surface for a minimum of four hours.

10

Mail completed form to testing laboratory within 24 hours of collection.

Schleicher & Schuell
P.O. Box 2012, Keene, NH 03431 • 1-800-345-4824 • FAX: 603-357-7100

Information provided by New York State Department of Health

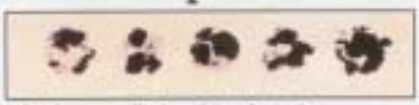
Simple Spot Check

Valid Specimen

Allow a sufficient quantity of blood to soak through to completely fill the preprinted circle on the filter paper. Fill all required circles with blood. Do not layer successive drops of blood or apply blood more than once in the same collection circle. Avoid touching or smearing spots.

Invalid Specimens

Possible Causes



1. Specimen quantity insufficient for testing.

- Removing filter paper before blood has completely filled circle or before blood has soaked through to second side.
- Applying blood to filter paper with a capillary tube.
- Touching filter paper before or after blood specimen collection with gloved or ungloved hands, hand lotion, etc.
- Allowing filter paper to come in contact with gloved or ungloved hands or substances such as hand lotion or powder, either before or after blood specimen collection.

2. Specimen appears scratched or abraded.

- Applying blood with a capillary tube or other device.

3. Specimen not dry before mailing.

- Mailing specimen before drying for a minimum of four hours.

4. Specimen appears supersaturated.

- Applying excess blood to filter paper, usually with a device.
- Applying blood to both sides of filter paper.

5. Specimen appears diluted, discolored or contaminated.

- Squeezing or "milking" of area surrounding the puncture site.
- Allowing filter paper to come in contact with gloved or ungloved hands, or substances such as alcohol, formula, antiseptic solutions, water, hand lotion or powder, etc., either before or after blood specimen collection.
- Exposing blood spots to direct heat.

6. Specimen exhibits serum rings.

- Not wiping alcohol from puncture site before making skin puncture.
- Allowing filter paper to come in contact with alcohol, hand lotion, etc.
- Squeezing area surrounding puncture site excessively.
- Drying specimen improperly.
- Applying blood to filter paper with a capillary tube.

7. Specimen appears clotted or layered.

- Touching the same circle on filter paper to blood drop several times.
- Filling circle on both sides of filter paper.

8. No blood.

- Failure to obtain blood specimen.

Schleicher & Schuell

Schleicher & Schuell, Inc. • 10 Optical Avenue • Keene, NH 03431

Manufacturer of 903 Specimen Collection Paper

Information provided by New York State Department of Health

There may be other tests besides those required in your state. More helpful information is available by contacting:

The National Newborn Screening and Genetics Resource Center

(512) 454-6419

www.genes-r-us.uthscsa.edu

or

Kentucky's Newborn Screening Program

(502) 564-3756 ext. 3761

http://chfs.ky.gov/dph/ach/newbornscreening.htm

U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration

These Tests Could Save Your Baby's Life

Newborn Screening Tests

Why does my baby need Newborn Screening tests?

Most babies are healthy when they are born.

We test all babies because a few babies look healthy but have a rare health problem.

If we find problems early, we can help prevent serious problems like mental retardation or death.

How will my baby be tested?

Before you leave the hospital, a nurse will take a few drops of blood from your baby's heel. The hospital will send the blood sample to a newborn screening lab.

How will I get the results of the test?

Parents are notified of test results if there is a problem.

Ask about results when you see your baby's health professional.

Why do some babies need to be retested?

Your baby may be retested if you leave the hospital before 24 hours.

Some States require a second test on all babies.

Some babies need to be retested because there is a problem with the blood sample.

A few babies need to be retested because the first test showed a possible health problem.

What if my baby needs to be retested?

Your baby's health professional or the State Health Department will contact you if your baby needs to be retested. They will tell you why the baby needs to be retested and what to do next.

If your baby needs to be retested, get it done right away.

Make sure that your hospital and health professional have your correct address and phone number.

What if I have questions?

Ask your baby's health professional if you have questions or concerns.

Qué puedo hacer si tengo preguntas?

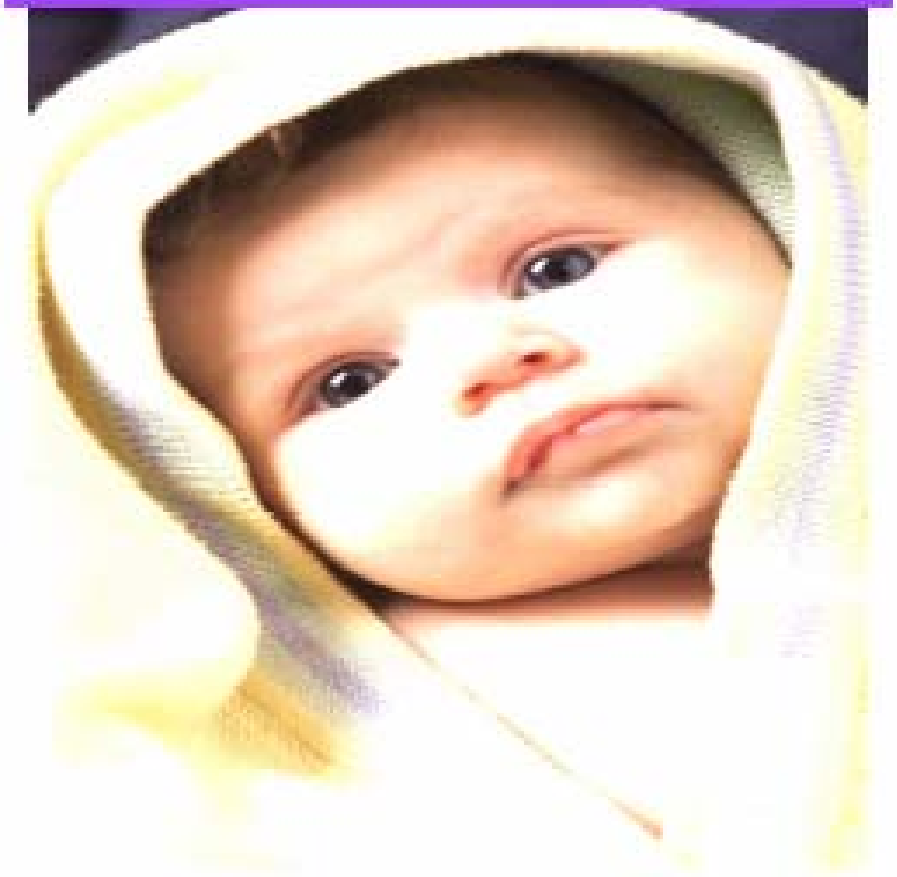
Si tiene preguntas o dudas, hable con el professional medico de su bebé.

Es posivle que haya preubas adicionales quie el departmento de salud de su estado no require. Para mas informacion en ingles, pongase en contacto con:

The National Newborn Screening and
Genetics Resource Center
(512) 454-6419
www.genes-r-us.uthscsa.edu
Or
Llame al porgrama de su estado
Kentucky's Newborn Screening Program
(502) 564-3756 ext. 3761
http://chfs.ky.gov/dph/ach/newbornscreening.htm

Esta Prueba Puede Slavar la Vida de su Bebé

Newborn Screening Tests



¿Por qué mi bebé necesita esta prueb a de sangre?

La mayoría de los bebés nacen sanos.

Le hacemos esta prueb a a todos los bebés porque a veces hay bebés que parecen sanos pero tienen un problema de salud raro.

?Cómo se hace la prueba?

Antes de que le den de alta a su bebé, un enfermero tomará unas gotas de sangre del talón de su bebé.

El hospital enviará la muestra de sangre a un laboratorio especializado.

¿Cómo obtendré los resultados de la prueba?

Si hay algún problema, usted será notificado de los resultados lo más antes posible.

Todos los resultados se envían al profesional médico de su bebé.

¿Por qué algunos bebé necesitan más pruebas?

Si le dan de alta a su bebé antes de las 24 horas, es posible que haya que repetir la prueba.

En algunos estados, todos los bebés recib en dos pruebas.

A veces se necesita otra muestra de sangre porque hubo problemas con la primera.

Otras veces se necesita otra muestra de sangre porque la primera mostró la posibilidad de un problema de salud.

¿Y si mi bebé necesita otra prueba?

Si su bebé necesita que se repita la prue ba, el profesional médico de su bebé o el departamento de salud del estado se pondrán en contacto con usted. Ellos le dirán por qué su bebé necesita otra prueba y lo que usted tiene que hacer.

Asegúrese que el hospital y su professional médico tengan su número de teléfono y dirección.

ERNIE FLETCHER
GOVERNOR

CABINET FOR HEALTH AND FAMILY SERVICES
DEPARTMENT FOR PUBLIC HEALTH
DIVISION OF
ADULT AND CHILD HEALTH IMPROVEMENT
275 EAST MAIN STREET, HS2W-C
FRANKFORT, KENTUCKY 40621
(502) 564-3756, (502) 564-1510 FAX

Mark D. Birdwhistell
Secretary

Laboratory Contact Information

YOU SHOULD RECEIVE AND OFFICIAL COPY OF THE NEWBORN SCREENING LAB RESULTS BUT SHOULD YOU NEED A COPY PLEASE FAX COMPLETED REQUEST FORM TO THE NUMBER BELOW:

FAX REQUEST FOR RESULTS: FAX # 502-564-2905

A COPY OF REQUEST FORM TO BE COMPLETED INCLUDED IN THIS BINDER.

TO ORDER SPECIMEN COLLECTION FORMS: 502-564-4446 EXT 4440

LABORATORY STAFF: 502-564-4446 EXT. 4434

Short Term Follow-Up (prior to university referral) Contact Information

Sandy Fawbush, RN: Phone: 502-564-3756 Ext. 3761
Troi Cunningham, RN 800-462-6122 Ext. 3761
Mary Sue Flora, RN sandy.fawbush@ky.gov

Newborn Screening Program Fax: 502-564-1510

PROVIDER FAX REQUEST
FOR LABORATORY INFORMATION

Date: _____

Please verify that all information below is completed accurately and legibly. We also request that you include a telephone number where you can be reached in the event we have questions and a fax number so you can receive the information you've requested. Thank you.

Infant Name: _____DOB: _____Sex: _____

Mother's Name: _____

Mother's SSN: _____

Requested Lab Values:_____

_____

Who is making this request?

PCP Name: _____

PCP Phone: (_____)_____

PCP Fax # (so request can be processed): _____

PCP Address: _____

_____

CONFIDENTIALITY NOTE: This facsimile message is intended only for the use of the individual or entity to which it is addressed and may contain confidential information that is legally privileged and exempt from disclosure and under applicable law. If the reader of this message is not the intended recipient, you are notified that any dissemination, distribution or copying of this communication is strictly prohibited. If you have received this communication in error, please notify us immediately by telephone and return same to us at the above address via the U.S. Postal Service. Thank you.

Newborn Screening Program

Resources for Metabolic Disorders

Amino Acid Disorders, Organic Acid and Fatty Acid Disorders

Clinic	Staff	Phone
University of Kentucky Lexington, KY **Primary Contact Number** **(859) 323-5404** Primary Contact Carol Reid MT (ASCP), MPA **Emergency after hours:** **(800) 888-5533** **(Page metabolic/newborn screening physician)**	Carol Reid, MT (ASCP), MPA C. Charlton Mabry, MD Carolyn Bay, MD Fax:(859) 323-8179	(859) 323-5404 (859) 323-5404 (859) 257-5559
University of Louisville Louisville, KY (502) 852-3879 **Primary Contact Number** **(502) 852-5334** **Emergency after hours: (502) 562-9914 beeper**	Joseph Hersh, MD MD After hours pager # Gordon Gowans, Alexander Asamoah, MD Karen Kinkus, RD Fax: (502) 852-7886	(502) 852-5334 (502) 562-9914 (502) 852-3879

Newborn Screening Program

Resources for Cystic Fibrosis

Clinic	Staff	Phone
University of Kentucky Division of Pediatric Pulmonology Carol Reid MT (ASCP), MPA **(859) 323-5404** **Emergency after hour:** **(800) 888-5533 (ask for pediatric pulmonology on call)**	Carol Reid, MT, (ASCP), MPA Michael Anstead, MD Jamshed F. Kanga, MD Fax: (859) 257-1888	(859) 323-5404 (859) 257-5536
University of Louisville Pediatric Pulmonary Medicine **(502) 629-8830** **Emergency after hours: (502) 629-6000** **(Page pediatric pulmonology)**	Martha Eddy, CPNP Ronald Morton, MD Nehm Eid, MD Fax: (502) 629-7540	(502) 629-8830 (502) 629-8830

Newborn Screening Program
Resources for Endocrinology

(Congenital Adrenal Hyperplasia, Congenital Hypothyroidism)

Clinic	Staff	Phone
University of Kentucky **(859) 323-5404** Dept. of Pediatrics Endocrinology and Metabolism Carol Reid MT, (ASCP), MPA **Emergency after hours: (800) 888-5533** **(ask for Pediatric Endocrinology)**	Carol Reid MT, (ASCP), MPA Jeff Lomenick, MD Jackson Smith, MD Fax: (859) 323-8179	(859) 323-5404 (859) 323-5404
University of Louisville **(502) 629-8821** Pediatric Endocrinology **Emergency after hours: 502-629-6000 or** **(800) 292-2759** **(Page pediatric endocrinology)**	Lee Ann Tincher, RN Michael Foster, MD Aaron Davis, MD Kellie Woodruff, ARNP Fax: (502) 629-8824	(502) 629-8821 (502) 629-8821

Newborn Screening Program

Resources for Hemoglobinopathies

(Hb S/S, Hb S/A, Hb S/C)

Clinic	Staff	Phone
University of Kentucky **Pediatric Hematology/Oncology** **Phone: (859) 323-8075** **Emergency after hours: (800) 888-5533** **(ask for pediatric hematology)**	Lisa Hess, ARNP Jeff Moscow, MD Fax: (859) 257-8978	(859) 323-8075 (859) 323-0239
University of Louisville **Pediatric Hematology/Oncology** **Phone (502) 629-7750** **Emergency after hours: (502) 629-6000** **(Page pediatric hematology)**	Diane Burnett, PNP Salvatore Bertelone, MD Fax: (502) 629-7784	(502) 629-7750 (502) 629-7750

Newborn Screening Program

Resources for Newborn Hearing and Screening

Location	Clinic	Consultant	Phone
Louisville, KY (877) 757-4327	Commission for Children with Special Health Care Needs 982 Eastern Parkway Louisville, KY 40217 (877) 757-4327	Karen Mercer, RN Michelle King (877) 757-4327 (HEAR) Ext. 258 (800) 232-1160 Ext. 323	
Central Region (800) 232-1160	Commission for Children with Special Health Care Needs 982 Eastern Parkway Louisville, KY 40217 (800) 232-1160	Eric Cahill (800) 232-1160 Ext. 322	
East Region (800) 817-3874	Commission for Children with Special Health Care Needs 333 Waller Ave. Ste 300 Lexington, KY 40504 (800) 817-3874	Lou Ann Jones (800) 817-3874 Ext. 225 Fax: (859) 225-7155	
West Region (800) 727-9903	Commission for Children with Special Health Care Needs 712 West 15th St. Hopkinsville, KY 42240 (800) 727-9903	Carolyn Kisler (800) 727-9903 Fax: (270) 889-6050	

DISORDERS

Test name	Test Abbreviation	Category
3-methylcrotonyl CoA Carboxylase deficiency	3MCC	Organic Acid Disorders
Argininosuccinic Acidemia	ASA	Amino Acid Disorders
Beta ketothiolase deficiency	BKT	Organic Acid Disorders
Biotinidase Deficiency	BIO	Other
Carnitine uptake defect	CUD	Fatty Acid Oxidation
Citrullinemia	CIT	Amino Acid Disorders
Congenital Adrenal Hyperplasia	CAH	Endocrine
Congenital Hypothyroidism	CH	Endocrine
Cystic Fibrosis	CF	Other
Galactosemia	GALT	Other
Glutaric acidemia type 1	GA-1	Organic Acid Disorders
Hemoglobin S-βeta thalassemia	Hb S/Th	Hemoglobin
Hemoglobin S/C disease	Hb S/C	Hemoglobin
Homocystinuria	HCY	Amino Acid Disorders
Hydroxymethylglutaric aciduria (3-OH 3-CH3 glutaric aciduria)	HMG	Organic Acid Disorders
Isovaleric acidemia	IVA	Organic Acid Disorders
Long-chain L-3hydroxyacyl-CoA dehydrogenase	LCHAD	Fatty Acid Oxidation
Maple Syrup Urine Disease	MSUD	Amino Acid Disorders
Medium-chain acyl-CoA dehydrogenase deficiency	MCAD	Fatty Acid Oxidation
Methylmalonic acidemia	Cbl A, B	Organic Acid Disorders
Methylmalonic acidemia mutase deficiency	MUT	Organic Acid Disorders
Multiple carboxylase deficiency	MCD	Organic Acid Disorders
Phenylketonuria	PKU	Amino Acid Disorders
Propionic Acidemia	PA	Organic Acid Disorders
Short-chain acyl-CoA dehydrogenase deficiency	SCAD	Fatty Acid Oxidation
Sickle cell disease	HB S/S	Hemoglobin
Trifunctional protein deficiency	TFP	Fatty Acid Oxidation
Tyrosinemia type I	TYR I	Amino Acid Disorders
Very long-chain acyl-CoA dehydrogenase deficiency	VLCAD	Fatty Acid Oxidation

Health Care Provider Fact Sheets

Disease Name — 3-methylcrotonyl-CoA carboxylase deficiency

Alternate name(s)	3-methylcrotonylglycinuria
Acronym	3-MCC
Disease Classification	Organic Acid Disorder
Variants	Late-onset form
Variant name	Late-onset 3-methylcrotonyl-CoA carboxylase deficiency
Symptom onset	Many individuals remain asymptomatic into adulthood. Others present in late infancy (generally after 3 months).
Symptoms	Infants can present with a Reye-like syndrome of ketoacidosis, hypoglycemia, hyperammonemia which can lead to seizures, coma and possibly death. Others present with failure to thrive, hypotonia or spasticity. Late-onset 3-MCC may present as developmental delay without Reye-like syndrome. Symptomatic adults often report general weakness and fatigue. Many individuals are asymptomatic.
Natural history without treatment	Primary manifestations appear to be muscular hypotonia and atrophy. Individuals with Reye-like illnesses may die or suffer neurologic insult during these episodes.
Natural history with treatment	Once over the initial crisis, most individuals have been intellectually normal. It is uncertain whether treatment modifies disease course.
Treatment	Protein restricted diet. Leucine-free medical foods. Possible carnitine supplementation. Giving treatment to asymptomatic individuals is of questionable value.
Other	Newborn screening has led to the diagnosis of asymptomatic women whose infants have transiently elevated isovalerylcarnitine.
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:50,000
Ethnic differences	No known population at increased risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Inner membrane of the mitochondria, liver and kidney.
Enzyme Function	Breakdown of leucine
Missing Enzyme	3-methylcrotonyl-CoA carboxylase
Metabolite changes	Increased 3-hydroxyisovaleric acid, increased 3-methylcrotonylglycine.
Gene	MCCA/MCCB
Gene location	3q25-q27, 5q12-q13.1
DNA testing available	Sequencing available internationally
DNA testing detail	No common mutations
Prenatal testing	May be possible for at-risk pregnancies using enzymatic analysis.
MS/MS Profile	C5:1 (tigyl or 3-methylcrotonyl carnitine) elevated C5-OH (3-hydroxy-2-methylbutyryl carnitine)- elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=210200
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

KentuckyUnbridledSpirit.com Kentucky UNBRIDLED SPIRIT An Equal Opportunity Employer M/F/D

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Argininosuccinic Acidemia

Alternate name(s)	Argininosuccinase deficiency, Argininosuccinic aciduria, Argininosuccinic acid lyase deficiency, Argininosuccinyl-CoA lyase deficiency ASL deficiency
Acronym	ASA or ASAL
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Late onset form
Symptom onset	Neonatal onset is typical, although later-onset may occur.
Symptoms	Anorexia, vomiting, lethargy, seizures and coma possibly leading to death.
Natural history without treatment	Mental and physical retardation due to hyperammonemia, cyclic vomiting, seizures, cerebral edema and trichorrhexis nodosa. Coma and death possible.
Natural history with treatment	Normal mental and physical development is possible if treatment is initiated before hyperammonemic crisis.
Treatment	Protein restricted diet, arginine supplementation to help complete the urea cycle, essential amino acid supplementation, ammonia scavenging drugs in some cases and supplemental carnitine if patient has a secondary deficiency.
Other	Enzyme is genetically heterogeneous and patients may present in infancy/childhood with MR or seizures.
Physical phenotype	Trichorrhexis nodosa (short, dry, brittle hair) in older patients.
Inheritance	Autosomal recessive
General population incidence	1:70,000
Ethnic differences	No
Population	N/A
Ethnic incidence	N/A
Enzyme location	Erythrocytes, liver and fibroblasts
Enzyme Function	Catalyzes the conversion of argininosuccinate to fumurate and arginine as part of the urea cycle.
Missing Enzyme	Argininosuccinate lyase
Metabolite changes	Hyperammonemia
Gene	ASL
Gene location	7q11.2
DNA testing available	No
DNA testing detail	No common mutation known. More than 25 mutations detected.
Prenatal testing	Enzyme assay in cultured amniocytes. DNA possible if mutations known. Analyte testing of amniocytes.
MS/MS Profile	Citrulline is elevated, may show elevated argininosuccinic peak.
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=207900
Genetests Link	www.genetests.org
Support Group	National Urea Cycle Disorders Foundation http://www.nucdf.org/ National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

KentuckyUnbridledSpirit.com Kentucky UNBRIDLED SPIRIT An Equal Opportunity Employer M/F/D

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Beta ketothiolase deficiency

Alternate name(s)	Alpha-methylacetoacetic aciduria, 2-methyl-3-hydroxybutyric acidemia, Mitochondrial acetoacetyl-CoA thiolase deficiency, MAT deficiency, T2 deficiency, 3-oxothiolase deficiency, 3-ketothiolase deficiency, 3-KTD deficiency
Acronym	BKD or BKT
Disease Classification	Organic Acid Disorder
Variants	No, but there is considerable clinical heterogeneity
Variant name	N/A
Symptom onset	Late infancy or childhood. Mean age at presentation is 15 months (range 3 days to 48 months). There are documented cases of asymptomatic patients with enzyme deficiency. Frequency of decompensation attacks falls with age and is uncommon after the age of 10.
Symptoms	Symptoms include intermittent episodes of severe metabolic acidosis and ketosis accompanied by vomiting (often hematemesis), diarrhea and coma that may progress to death. There is great clinical heterogeneity between patients. Infancy is the period of highest risk for decompensation. Death or neurologic complications can occur. Neurologic damage includes striatal necrosis of the basal ganglia, dystonia and/or mental retardation. Other symptoms include cardiomyopathy, prolonged QT interval, neutropenia, thrombocytopenia, poor weight gain, renal failure and short stature. If neurologically intact, patients are normal between episodes.
Natural history without treatment	Clinical outcome varies widely with a few patients suffering severe psychomotor retardation or death as a result of their initial attack and others with normal development and no episodes of acidosis.
Natural history with treatment	Despite severe recurrent attacks, appropriate supportive care can result in normal development.
Treatment	Avoidance of fasting. Bicarbonate therapy and intravenous glucose in acute crises. Possible protein restriction. Consider carnitine supplementation.
Other	N/A
Physical phenotype	No dysmorphisms
Inheritance	Autosomal recessive
General population incidence	unknown
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	Converts 2-methylacetoacetyl-CoA to propionyl-CoA and acetyl-CoA.
Enzyme Function	Catalyzes the decarboxylation of oxoacids.
Missing Enzyme	Mitochondrial acetoacetyl-CoA thiolase enzyme
Metabolite changes	Increased urinary excretion of 2-methyl-3-hydroxybutyric acid, 2-methylacetoacetic acid, tiglylglycine, 2-butanone, and ketone bodies (acetoacetic acid, 3-hydroxybutyric acid).
Gene	ACAT1
Gene location	11q22.3-q23.1
DNA testing available	Not in US. Sequencing of gene on a research basis.
DNA testing detail	No common mutation known
Prenatal testing	Enzyme analysis in amniocytes or CVS tissue. If mutations have been identified, DNA testing is possible.
MS/MS Profile	C5:1 tiglycarnitine – elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203750
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Biotinidase Deficiency

Alternate name(s)	Multiple carboxylase deficiency, late-onset multiple carboxylase deficiency, juvenile-onset BTD deficiency
Acronym	BTD
Disease Classification	Metabolic Disorder
Symptom onset	Prior to 12 months of age
Symptoms	In the untreated state, profound biotinidase deficiency during infancy is usually characterized by neurological and cutaneous findings that include seizures, hypotonia, and rash, often accompanied by hyperventilation, laryngeal stridor, and apnea. Older children may also have alopecia, ataxia, developmental delay, neurosensory hearing loss, optic atrophy, and recurrent infections. Individuals with partial biotinidase deficiency may have hypotonia, skin rash, and hair loss, particularly during times of stress. All symptomatic children improve when treated with 5 to 10 mg of oral biotin per day.
Natural history without treatment	Prolonged symptoms prior to institution of biotin therapy may leave the patient with varying degrees of neurological sequelae, including mental retardation, seizures, and coma. Death may result from untreated profound biotinidase deficiency.
Natural history with treatment	If treated promptly, biotinidase deficiency may be asymptomatic.
Treatment	Biotin supplement daily
Inheritance	Autosomal recessive
General population incidence	1:60,000 estimated with either profound or partial deficiency
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=253260
Genetests Link	www.geneclinics.org
Support Group	Biotinidase Family Support Group http://biotinidasedeficiency.20m.com/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Carnitine uptake defect

Alternate name(s)	Systemic carnitine deficiency, Carnitine deficiency, Carnitine transporter deficiency
Acronym	SCD, CUD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	N/A
Variant name	N/A
Symptom onset	Infancy or childhood with fasting hypoglycemia, weakness and/or cardiomyopathy.
Symptoms	Hypoketotic hypoglycemia, seizures, vomiting, lethargy progressing to coma. Chronic muscle weakness, cardiomyopathy, hepatomegaly.
Natural history without treatment	Non-progressive developmental delay due to hypoglycemia, cardiomyopathy and muscle weakness.
Natural history with treatment	Developmental delay, if present, is not reversed by treatment. Cardiomyopathy and muscle weakness can be reversed by treatment.
Treatment	Carnitine supplementation, no fasting.
Other	N/A
Physical phenotype	Cardiomyopathy, muscle weakness.
Inheritance	Autosomal recessive
General population incidence	1/40,000
Ethnic differences	No
Population	N/A
Ethnic incidence	N/A
Enzyme location	Muscle, heart, kidney, leukocytes and fibroblasts
Enzyme Function	Transports carnitine into cells
Missing Enzyme	Carnitine transporter
Metabolite changes	Decreased free carnitine in plasma, increased carnitine in urine, decreased carnitine in muscle.
Gene	SLC22A5
Gene location	5q33.1
DNA testing available	May be available on a research basis.
DNA testing detail	If a mutation in a proband is detected, DNA carrier screening is possible.
Prenatal testing	Protein analysis in cultured amniocytes, biochemical analyte testing. If a mutation in a proband is detected, DNA prenatal diagnosis via CVS or amniocytes is possible.
MS/MS Profile	Reduced concentrations of free carnitine and various acylcarnitine species.
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=212140
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Citrullinemia

Alternate name(s)	Argininosuccinic acid synthetase deficiency
Acronym	ASAS or CIT
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Citrullinemia type II (adult and neonatal onset forms) – caused by *SLC25A13* mutations
Symptom onset	Neonatal with some variability
Symptoms	Potential lethal coma, seizures, anorexia, vomiting, lethargy, apnea and hypertonia. Possible enlarged liver.
Natural history without treatment	Mental retardation due to hyperammonemia.
Natural history with treatment	Normal IQ and development are possible if no damage from initial or subsequent hyperammonemic episodes.
Treatment	Management of hyperammonemic cases with sodium benzoate and/or phenylacetate and arginine. Dietary restriction of protein, arginine and essential amino acid supplementation.
Other	N/A
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	Rare
Ethnic differences	Yes
Population	Citrullinemia type II is common in Japan
Ethnic incidence	N/A
Enzyme location	Widely expressed in tissues; liver, kidney and fibroblasts.
Enzyme Function	Catalyzes the conversion of citrulline and aspartic acid to argininosuccinic acid.
Missing Enzyme	Argininosuccinic acid synthetase
Metabolite changes	Hyperammonemia
Gene	CTLN1
Gene location	9q34
DNA testing available	Yes
DNA testing detail	Linkage analysis
Prenatal testing	Linkage analysis and enzyme testing
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=215700
Genetests Link	www.genetests.org
Support Group	National Urea Cycle Disorders Foundation http://www.nucdf.org/ National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	**Congenital Adrenal Hyperplasia**
Acronym	CAH
Disease Classification	Endocrine Disorder
Symptom onset	Infants with CAH do not appear ill at birth, but may, within the first few weeks of life, experience a salt-losing crisis which can lead to serious illness and death.
Symptoms	Congenital adrenal hyperplasia (CAH) results from a deficiency in one or another of the enzymes of cortisol biosynthesis. In about 95% of cases, 21-hydroxylation is impaired in the adrenal cortex so that 17-hydroxyprogesterone (17-OHP) is not converted to 11-deoxycortisol. Because of defective cortisol synthesis, ACTH levels increase, resulting in overproduction and accumulation of cortisol precursors, particularly 17-OHP, proximal to the block. This causes excessive production of androgens, resulting in virilization.
Natural history without treatment	If untreated, children with CAH will experience abnormally rapid growth early in childhood (but stunted in the long run) and early appearance of body hair. Babies with the salt-wasting form of CAH (about 75 percent of cases) are at risk for rapid, uncontrolled loss of salt from the body that can result in death. The imbalance of hormones before birth may cause some girls to have ambiguous genitalia.
Treatment	Daily supplements of the hormone cortisol, and in many cases a salt-retaining hormone. To prevent problems, treatment must begin shortly after birth.
Physical phenotype	Ambiguous genitalia in females
Inheritance	Autosomal recessive
General population incidence	1 in 21,500
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=201910
Genetests Link	www.genetests.org
Support Group	Congenital Adrenal Hyperplasia Research Education & Support http://www.caresfoundation.org MAGIC Foundation for Children's growth (MAGIC) http://www.magicfoundation.org National Organization for Rare Diseases http://www.rarediseases.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	Congenital Hypothyroidism
Acronym	CH
Disease Classification	Endocrine Disorder
Symptom onset	Clinical signs of hypothyroidism often do not appear until the infant is 3-4 months of age. Thus, it is most likely that affected infants will have already suffered irreversible brain damage before signs of the disease begin to appear. Many times the early diagnosis relies almost solely on the results of the newborn screening.
Symptoms	An affected infant may have prolonged neonatal jaundice, growth failure, lethargy, poor appetite and constipation.
Natural history without treatment	Even mild hypothyroidism can lead to severe mental retardation and growth retardation if untreated. Development is delayed early on, often indicated by failure to meet normal milestones.
Treatment	Daily oral thyroxine medication to prevent problems, treatment must begin shortly after birth and is lifelong.
Inheritance	Although this disorder is detectable at birth, it is not an inherited disorder. Hypothyroidism does not follow any type of pattern as to whom it will affect and randomly affects infants from almost every origin.
General population incidence	Estimated to affect 1 in 4,500 births
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=201910
Genetests Link	www.genetests.org
Support Group	MAGIC Foundation for Children's growth (MAGIC) http://www.magicfoundation.org National Organization for Rare Diseases http://www.rarediseases.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	**Cystic Fibrosis**
Acronym	CF
Disease Classification	Genetic Disorder Formerly known as cystic fibrosis of the pancreas, this entity has increasingly been labeled simply 'cystic fibrosis.' Manifestations relate not only to the disruption of exocrine function of the pancreas but also to intestinal glands (meconium ileus), biliary tree (biliary cirrhosis), bronchial glands (chronic bronchopulmonary infection with emphysema), and sweat glands (high sweat electrolyte with depletion in a hot environment). Infertility occurs in males and females.
Symptom onset	Usually within the first year of life. A small number, however, are not diagnosed until age 18 or older. These patients usually have a milder form of the disease.
Symptoms	Infants with CF have a variety of symptoms including: meconium ilieus, liver disease, pancreatic insufficiency, pulmonary disease or an excessive appetite but poor weight gain; and greasy, bulky stools. Symptoms vary from person to person due, in part, to the more than 1,000 mutations of the CF gene. The sweat test is the standard diagnostic test for CF. A sweat test should be performed at a CF Foundation-accredited care center where strict guidelines are followed to ensure accurate results. This simple and painless procedure measures the amount of salt in the sweat. A high salt level indicates CF.
Treatment	The treatment of CF depends upon the stage of the disease and the organs involved. Clearing mucus from the lungs is an important part of the daily CF treatment regimen. In addition, approximately 90 percent of all people with CF take pancreatic enzyme supplements to help them absorb food in digestion.
Inheritance	Autosomal recessive
General population incidence	1 in 2,500 white live births and 1 in 17,000 African American live births.
OMIM Link	http://www3.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=219700
Genetests Link	www.genetests.org
Support Group	Cystic Fibrosis Foundation http://www.cff.org/home National Organization for Rare Diseases http://www.rarediseases.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	**Galactosemia**
Acronym	GALT
Disease Classification	Disorder of carbohydrate metabolism
Variants	Yes
Variant name	Duarte galactosemia
Symptom onset	Infancy
Symptoms	The affected infant may appear normal at birth. Within a few days to two weeks after initiating milk feedings, the infant develops vomiting, diarrhea, lethargy, jaundice, and liver damage. Untreated, the disorder may result in death, frequently associated with E. coli septicemia. Infants surviving the above symptoms may evidence developmental retardation, hepatomegaly, Fanconi's syndrome, growth failure and cataracts.
Natural history without treatment	If not detected immediately, it results in liver disease, cataracts, mental retardation, and even death. Death can occur as early as one to two weeks of age from severe escherichia (E. coli) bacteria infections. E. coli infections are common in untreated galactosemic infants. The American Liver Foundation recommends that all infants who develop jaundice be considered for galactosemia.
Natural history with treatment	As Galactosemic children get older they may encounter delays in speech and females may suffer from ovarian failure. Nevertheless, children who are diagnosed early have very good long-term outlooks and will lead normal, healthy lives.
Treatment	Treatment for galactosemia is the elimination of galactose and lactose from the diet throughout life. Infants are places on soy formula.
Physical phenotype	No abnormalities present at birth.
Inheritance	Autosomal recessive
General population incidence	1:65,000 live births
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=606999
Genetests Link	www.geneclinics.org
Support Group	Parents of Galactosemic Children, Inc. http://www.galactosemia.org Children's Liver Alliance http://www.liverkids.org.au Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Glutaric acidemia, type 1

Alternate name(s)	Glutaric aciduria I, Glutaryl-CoA dehydrogenase deficiency
Acronym	GA1, GAI
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Riboflavin responsive GA1
Symptom onset	Infancy (typically 2- 37 months)
Symptoms	Macrocephaly may be present at birth, acute encephalitic-like crises; neurodegenerative disorder with spasticity, dystonia, choreoathetosis, ataxia and dyskinesia, seizures, hypotonia, death due to Reye-like syndrome.
Natural history without treatment	Possible developmental delay due to encephalitis-like crisis; neurologic deterioration including spasticity, dystonic cerebral palsy. May have neurologic signs with normal IQ. Some individuals may be asymptomatic.
Natural history with treatment	If instituted before any damage occurs, normal outcome may occur. Risk for neurologic damage is highest in first few years. Some evidence that treatment may slow neurologic deterioration.
Treatment	Lysine and tryptophan restricted diet, riboflavin supplementation, carnitine supplementation. Rapid treatment of intercurrent illness with intravenous glucose, carnitine and appropriate supportive measures.
Other	Profuse sweating has been reported. Neuroradiographic findings of frontotemporal atrophy on CT or MRI with increased CSF containing spaces in the sylvian fissures and anterior to the temporal lobes. Also decreased attenuation in cerebral white matter on CT and increased signal intensity on MRI. Basal ganglia changes.
Physical phenotype	Macrocephaly, cerebral palsy
Inheritance	Autosomal recessive
General population incidence	1:40,000 in Caucasians and 1:30,000 in Sweden
Ethnic differences	Yes
Population	Old Amish and Ojibway Indians in Canada
Ethnic incidence	1/10 carrier frequency
Enzyme location	Mitochondria; liver, kidney, fibroblasts and leukocytes
Enzyme Function	Metabolizes lysine, hydroxylysine and tryptophan
Missing Enzyme	Glutaryl-CoA dehydrogenase
Metabolite changes	Increased glutaric acid in urine, increased glutaric acid and 3-hydroxyglutaric acid in plasma, 3-hydroxyglutaric and glutaconic acid in urine.
Gene	GCDH
Gene location	19p13.2
DNA testing available	Yes.
DNA testing detail	No common mutations outside of Old Amish (A421V)
Prenatal testing	Enzyme activity in CVS and amniocytes
MS/MS Profile	Elevated C5DC - can be missed some patients
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=231670
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Hemoglobin S-β Thalassemia Disease

Alternate Name(s) Beta Thalassemia Sickle Disease
Acronym Hb β/S
Disease Classification Hemoglobinopathy

Infants whose hemoglobin does not produce enough beta protein have beta thalassemia. It is found in people of Mediterranean descent, such as Italians and Greeks, and is also found in the Arabian Peninsula, Iran, Africa, Southeast Asia and southern China. There are three types of beta thalassemia that also range from mild to severe in their effect on the body.
Thalassemia Minor or *Thalassemia Trait*. In this condition, the lack of beta protein is not great enough to cause problems in the normal functioning of the hemoglobin. A person with this condition simply carries the genetic trait for thalassemia and will usually experience no health problems other than a possible mild anemia.
Thalassemia Intermedia. In this condition the lack of beta protein in the hemoglobin is great enough to cause a moderately severe anemia and significant health problems, including bone deformities and enlargement of the spleen. However, there is a wide range in the clinical severity of this condition, and the borderline between thalassemia intermedia and the most severe form, thalassemia major, can be confusing. The deciding factor seems to be the amount of blood transfusions required by the patient. The more dependent the patient is on blood transfusions, the more likely he or she is to be classified as thalassemia major. Generally speaking, patients with thalassemia intermedia need blood transfusions to improve their quality of life, but not in order to survive.
Thalassemia Major or *Cooley's Anemia***.** This is the most severe form of beta thalassemia in which the complete lack of beta protein in the hemoglobin causes a life-threatening anemia that requires regular blood transfusions and extensive ongoing medical care. These extensive, lifelong blood transfusions lead to iron-overload which must be treated with chelation therapy to prevent early death from organ failure.

Symptoms Most children with thalassemia major appear healthy at birth, but during the first year or two of life they become pale, listless and fussy, and have a poor appetite. They grow slowly and often develop jaundice (yellowing of the skin).

Natural history without treatment The spleen, liver, and heart soon become greatly enlarged. Bones become thin and brittle; face bones become distorted, and children with thalassemia often look alike. Heart failure and infection are the leading causes of death among children with untreated thalassemia major. Children with thalassemia intermedia may develop some of the same complications, although in most cases, the course of the disease is mild for the first two decades of life.

Treatment

Red Blood Cell Transfusion
Because there is no natural way for the body to eliminate iron, the iron in the transfused blood cells builds up in a condition known as "iron overload" and becomes toxic to tissues and organs, particularly the liver and heart. Iron overload typically results in the patient's early death from organ failure.
Chelation Therapy: To help remove excess iron, patients undergo the difficult and painful infusion of a drug, Desferal. Reduced mortality and morbidity with appropriate penicillin prophylaxis.

Inheritance Autosomal recessive
General population incidence 1:250,000
Genetests Link www.geneclinics.org
Support Group Cooley's Anemia Foundation
http://www.cooleysanemia.org/
Sickle Cell Information Center
http://www.scinfo.org/
Sickle Cell Disease Association of America, Inc.
http://www.sicklecelldisease.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	Hemoglobin S/C Disease
Alternate Name(s)	Sickle Cell Hemoglobin C Disease
Acronym	Hb S/C
Disease Classification	Hemoglobinopathy
Symptom onset	May be asymptomatic.
Symptoms	Any sign of illness in an infant with sickling disease is a potential medical emergency. Acute and chronic tissue injury can occur when sickled cells cause vascular occlusion. Sickling diseases can cause severe pain anywhere in the body, but most often in the hands, arms, chest, legs and feet. Complications may include, but are not limited to, the following: sepsis, acute chest syndrome, hand-and-foot syndrome, splenic sequestration crisis, aplastic crisis, stroke and painful episodes.
Natural history without treatment	Infants with hemoglobin C disease are vulnerable to serious bacterial infections that can be life threatening.
Natural history with treatment	Reduced mortality and morbidity with penicillin prophylaxis.
Treatment	The National Institutes of Health clinical guidelines for management of sickle cell disease state, "Penicillin prophylaxis should begin by 2 months of age for infants with suspected sickle cell anemia, whether or not the definitive diagnosis has been established." Antibiotic therapy should continue until at least 5 years of age.
Inheritance	Autosomal recessive
General population incidence	Affects 2 to 3% of African American in the United States.
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=603903
Genetests Link	www.geneclinics.org
Support Group	Sickle Cell Information Center http://www.scinfo.org/ Sickle Cell Disease Association of America, Inc. http://www.sicklecelldisease.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name **Homocystinuria**

Alternate name(s)	Cystathionine beta-synthase deficiency
Acronym	CBS deficiency
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Pyridoxine-responsive type (the majority of cases are unresponsive to pyridoxine)
Symptom onset	Childhood
Symptoms	Ectopia lentis, vascular occlusive disease, seizures, malar flush, osteoporosis, possible decreased pigmentation of hair, skin and iris, skeletal abnormalities including genu valgum, pectus excavatum, pes cavus and marfanoid habitus. Some patients have failure to thrive and short stature. Mental retardation is possible.
Natural history without treatment	Mental retardation is common but not invariable. Vascular disease, stroke and psychiatric abnormalities.
Natural history with treatment	Decrease of thromboembolic accidents which may decrease incidence of sequelae including mental retardation, ectopia lentis, seizures and psychiatric abnormalities. Normal IQ is possible and typical of the pyridoxine-responsive variant.
Treatment	Pyridoxine supplementation, dietary restriction of methionine with supplementation of L-cysteine, betaine supplementation. Consider folate and vitamin B12 supplementation.
Other	N/A
Physical phenotype	Ectopia lentis, decreased pigmentation, malar flush, osteoporosis, skeletal abnormalities and marfanoid habitus
Inheritance	Autosomal recessive
General population incidence	1:200,000 – 300,000
Ethnic differences	Yes
Population	Irish, U.S New England
Ethnic incidence	1:50,000
Enzyme location	Lymphocytes, fibroblasts and liver
Enzyme Function	Degradation of homocysteine
Missing Enzyme	Cystathionine beta-synthase
Metabolite changes	Increased methionine in blood, increased homocystine in urine, increased total homocysteine in blood.
Gene	CBS gene
Gene location	21q22.3
DNA testing available	Yes
DNA testing detail	Numerous mutations have been detected. Most prevalent mutations are G307S and I278T. Most patients are compound heterozygotes.
Prenatal testing	Enzyme assay in cultured amniocytes (CVS not possible)
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=236200
Genetests Link	www.genetests.org
Support Group	National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	**Hydroxymethylglutaric aciduria (3-OH 3-CH3 glutaric aciduria)**
Acronym	HMG-CoA lyase deficiency or HMG
Disease Classification	Organic Acid Disorder
Variants	No
Variant name	N/A
Symptom onset	Infancy (6 months to 2 years)
Symptoms	Persistent vomiting, lethargy, hypotonia, coma, seizures, apnea, hepatomegaly.
Natural history without treatment	Recurrent episodes of acute illness usually in response to fasting or to viral infection. Any episode can lead to death or developmental delay if severe enough.
Natural history with treatment	Normal IQ and development are possible. Severe hypoglycemic episodes may result in seizures and mental retardation.
Treatment	Avoidance of fasting. Low fat, protein and high carbohydrate diet. Cornstarch supplementation. Carnitine supplementation. Intravenous glucose to treat hypoglycemia during crisis episodes.
Other	Crises consist of severe acidosis and hypoglycemia treated with IV glucose and bicarbonate administration.
Physical phenotype	Possible microcephaly
Inheritance	Autosomal recessive
General population incidence	Rare
Ethnic differences	No
Population	N/A
Ethnic incidence	N/A
Enzyme location	Liver, fibroblasts and leukocytes
Enzyme Function	Catalyzes the final step of leucine degradation and plays a role in ketone formation.
Missing Enzyme	HMG CoA lyase
Metabolite changes	3-hydroxy-3-methylglutaric acid in urine, increased levels of glutaric and adipic acids may be elevated in urine during crisis, notable absence of ketosis.
Gene	HMGCL
Gene location	1pter-p33
DNA testing available	No
DNA testing detail	N/A
Prenatal testing	Prenatal testing has been accomplished by analysis of metabolites in maternal urine at 23 weeks. Enzyme is active in amniocytes and prenatal testing should be possible using this method.
MS/MS Profile	N/A
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=231670
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Isovaleric acidemia

Alternate name(s)	Isovaleric acid CoA dehydrogenase deficiency
Acronym	IVA
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Chronic intermittent form
Symptom onset	Infancy (in the acute neonatal form). The chronic intermittent form presents later in infancy or in childhood.
Symptoms	Episodic overwhelming illness with vomiting, ketosis, acidosis and coma. Hematological abnormalities include leucopenia, thrombocytopenia and possible anemia.
Natural history without treatment	About 50% of patients with the acute neonatal form will die during their first episode. Survivors may have neurological damage though several have made complete recoveries. Patients with the chronic form may have neurologic damage, but the majority of patients are developmentally normal.
Natural history with treatment	Intellectual prognosis depends on early diagnosis and treatment and subsequently on long-term compliance. If treated appropriately, most will have normal development.
Treatment	Low protein diet with restricted leucine intake, glycine supplementation and possible carnitine supplementation.
Other	Sometimes a “sweaty feet” odor is reported during an acute crisis.
Physical phenotype	No obvious dysmorphic features.
Inheritance	Autosomal recessive
General population incidence	1:230,000
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	N/A
Enzyme Function	Isovaleryl-CoA dehydrogenase is the first step in the branched chain organic acid metabolism of leucine.
Missing Enzyme	Isovaleryl-CoA dehydrogenase
Metabolite changes	Urinary isovaleryl glycine, 3-hydroxysoraline acid, increased isovaleric acid in blood. During acute attacks, 4-hydroxyisovaleric acid, mesaconic acid, and methylsuccinic acid, isovalerylglycine and 3-hydroxyisovaleric acid are present.
Gene	IVD
Gene location	15q14-15
DNA testing available	No
DNA testing detail	N/A
Prenatal testing	Enzyme analysis by GCMS in amniotic fluid or CVS tissue.
MS/MS Profile	Elevated C5 isovaleryl carnitine
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=243500
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency

Alternate name(s)	N/A
Acronym	LCHADD, TFP or LCHAD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	Mitochondrial trifunctional protein deficiency
Symptom onset	Neonatal, infancy
Symptoms	Hypoketotic hypoglycemia, hypotonia, cardiomyopathy, hepatic disease, peripheral neuropathy and pigmentary retinopathy, rhabdomyolysis, sudden death
Natural history without treatment	Possible developmental delay due to damage from hypoglycemic episodes, possible death due to cardiomyopathy or hepatic failure.
Natural history with treatment	Intelligence is usually normal if there is no damage due to hypoglycemic crisis. Peripheral neuropathy, if present, may not improve with treatment.
Treatment	Avoidance of fasting, use of uncooked starch, MCT treatments, carnitine supplementation, DHA supplementation (may prevent retinopathy, but this has not been proven)
Other	Maternal complications in pregnancy include acute fatty liver of pregnancy, HELLP syndrome, and pre-eclampsia
Physical phenotype	Hypotonia, cardiomyopathy and possible retinal changes
Inheritance	Autosomal recessive
General population incidence	Rare
Ethnic differences	Yes
Population	Finnish
Ethnic incidence	1:240 carrier rate for common mutation G1528C in Finland
Enzyme location	Inner mitochondrial membrane, liver, heart, fibroblasts
Enzyme Function	Metabolizes long chain fatty acids (C-12 to C-16 in length)
Missing Enzyme	Long-chain 3-hydroxyacyl-CoA dehydrogenase or mitochondrial trifunctional protein
Metabolite changes	Increased 3-hydroxydicarboxylic acids in urine, increased saturated and unsaturated 3-hydroxy organic acids, possible elevated CPK during acute illness.
Gene	HADHA and HADHB (alpha and beta subunits)
Gene location	2p23
DNA testing available	Yes – mutation analysis
DNA testing detail	Common mutation, G1528C, accounts for 87% of all mutant alleles in LCHAD deficiency; 70% of affected individuals will be homozygous for this mutation. There is no common mutation in trifunctional protein deficiency.
Prenatal testing	Enzyme analysis, protein analysis and direct DNA (when applicable).
MS/MS Profile	C18:OH, C16:1OH, C16OH
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=600890
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Maple syrup urine disease

Alternate name(s)	Branched chain ketoaciduria, Branched chain alpha-keto dehydrogenase deficiency
Acronym	MSUD type 1A, BCKD deficiency
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	MSUD type 1B, MSUD Type II, Intermittent branched-chain ketoaciduria, Intermediate branched-chain ketoaciduria, Thiamine responsive MSUD
Symptom onset	Neonatal with some variability
Symptoms	Lethargy progressive to coma and possible death, vomiting, difficulty feeding, hypoglycemia, possible high pitched cry.
Natural history without treatment	Neurologic abnormalities and profound mental retardation.
Natural history with treatment	Normal IQ and development may be expected if treatment is initiated before first crisis, but development is delayed in the severest cases.
Treatment	Dietary restriction of the branched chain amino acids and supplementation with medical formula. Thiamine supplementation in thiamine responsive patients.
Other	“Maple syrup”-like odor to urine (usually present during crisis)
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:200,000
Ethnic differences	Yes
Population	Mennonites, French-Canadians
Ethnic incidence	1/760 (Mennonites)
Enzyme location	Inner mitochondrial membrane; liver, kidney, leukocytes and fibroblasts.
Enzyme Function	Catalyzes the decarboxylation of oxoacids.
Missing Enzyme	Branched-chain ketoacid dehydrogenase (BCKAD). This enzyme is a multienzyme complex with 3 components – E1, E2 and E3.
Metabolite changes	Increased leucine, isoleucine and valine in plasma and urine, increased organic acids in urine.
Gene	Four genes are involved in formation of multicomplex enzyme.
Gene location	E1alpha = 19q13.1-13.2 E1beta = 6p21-22 E2 = 1p31 E3=7q31-32
DNA testing available	Yes
DNA testing detail	Common mutation present in Mennonites (Y393N-alpha) and comprehensive DNA mutation analysis.
Prenatal testing	Enzyme testing by CVS or amnio. If mutation is known, DNA testing may be available.
MS/MS Profile	Leucine elevated, leucine to alanine ratio elevated.
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=248600
Genetests Link	www.genetests.org
Support Group	The MSUD Family Support Group http://www.msud-support.org National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Medium-chain acyl-CoA dehydrogenase deficiency

Alternate name(s)	None
Acronym	MCADD or MCAD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	N/A
Variant name	N/A
Symptom onset	Typically 6-24 months but ranges from neonatal to adult
Symptoms	Recurrent episodes of hypoglycemia, vomiting, coma, sudden death and possible seizures. Hepatomegaly usually present.
Natural history without treatment	Metabolic episodes can cause developmental and physical delays, neurologic impairment and sudden death.
Natural history with treatment	Normal intellect and physical functioning expected.
Treatment	Dietary: avoid fasting, low-fat diet (<30% of dietary fat), carnitine supplementation, cornstarch supplementation.
Other	N/A
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1/15,000
Ethnic differences	Yes
Population	Incidence higher in Northern Europeans and U.S Caucasians.
Ethnic incidence	Approximately 1/70 carrier rate
Enzyme location	Liver, heart, muscle and fibroblasts
Enzyme Function	Mitochondrial beta-oxidation of fat stores
Missing Enzyme	Medium-chain acyl-CoA dehydrogenase
Metabolite changes	Increased medium chain fatty acids, increased glycine/carnitine esters, increased dicarboxylic acids.
Gene	ACADM
Gene location	1p31
DNA testing available	Yes
DNA testing detail	One mutation K304E (985A) accounts for majority of disease incidence, 80% of affected individuals are homozygous for this mutation and 18% of affected individuals are heterozygous.
Prenatal testing	DNA and enzymatic testing
MS/MS Profile	Elevated C10:1, C8, C6
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=201450
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Organic Acidemia Association Http://www.oaanews.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Methylmalonic acidemia

Alternate name(s)	Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in adenosylcobalamin, cblA complementation type; Methylmalonic acidemia, cblA type; Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in synthesis of adenosylcobalamin, cbl B complementation type
Acronym	MMA, MMAA/MMAB or CblA,B
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Methylmalonic acidemia, Vitamin B-12 non-responsive; Combined deficiency of methylmalonyl-CoA mutase and homocysteine
Symptom onset	Variable. Ranges from the first days of life to completely asymptomatic.
Symptoms	Episodic ketoacidosis with vomiting accompanied by lethargy and coma which can lead to death. Survivors can have developmental delays, growth retardation, spastic quadriparesis, dystonia and seizures. Neutropenia, thrombocytopenia and osteoporosis are common complications.
Natural history without treatment	Variable depending on the enzyme defect. Some will die in the newborn period, others will survive with deficits and others will be asymptomatic.
Natural history with treatment	**CblA:** Good prognosis with injections of hydroxy-cobalamin (OH-cbl) which reverses biochemical and clinical abnormalities in about 90% of patients. **CblB:** Equal fractions of affected patients are alive and well, alive and impaired, or deceased. The age of onset of symptoms can help prognosticate outcome – those patients with a later onset of symptoms have a more benign course. Approximately 40% of patients will respond with a drop in MMA level when given OH-cbl injections.
Treatment	Protein restricted diet, OH-cbl injections, carnitine supplementation, oral antibiotic therapy to decrease proprionate and medical foods. Liver transplant or combined liver/kidney transplant may increase metabolic control, but may not prevent neurologic complications.
Other	N/A
Physical phenotype	Minor facial dysmorphisms including high forehead, broad nasal bridge, epicanthal folds, long, smooth philtrum and triangular mouth. A variety of skin lesions can be seen in patients due to moniliasis.
Inheritance	Autosomal recessive
General population incidence	1:48,000
Ethnic differences	No known population at increased risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondria
Enzyme Function	Production of adenosylcobalamin
Missing Enzyme	Cobalamin A (cblA) deficiency: cobalamin reductase Cobalamin B (cblB) deficiency: cobalamin adenosyltransferase
Metabolite changes	Elevated glycine in urine
Gene	MMAA (cobalamin A disease) MMAB (cobalamin B disease)
Gene location	MMAA: 4q31.1-q31.2 MMAB: 12q24
DNA testing available	Sequencing available internationally
DNA testing detail	N/A
Prenatal testing	Possible via enzyme assay on amniocytes or CVS.
MS/MS Profile	Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine.
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=251000
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org Fatty Oxidation Disorder (FOD) Family Support Group www.fodsupport.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Methylmalonic acidemia mutase deficiency

Alternate name(s)	Methylmalonic aciduria due to methylmalonic CoA mutase deficiency, methylmalonic acidemia deficiency Vitamin B-12 non-responsive, Complementation group mut0, Methylmalonyl-CoA mutase
Acronym	MMA
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Vitamin B12 metabolic defect with methylmalonic acidemia and homocystinuria
Symptom onset	Eighty percent of infants become ill during the first week or life and 90% will present by the end of the first month. Infants with the less severe *mut-* may present later than the first month. A few may remain asymptomatic or present much later in life depending on the residual enzyme activity and the metabolic stressors.
Symptoms	Most common signs and symptoms are lethargy, failure to thrive, recurrent vomiting, dehydration which leads to profound metabolic acidosis, respiratory distress, hypotonia and death if not recognized. Complications of acute episodes can include metabolic stroke, extrapyramidal signs, dystonia and bilateral lucencies of globus pallidus. Survivors may have significant neurological damage. Renal failure may appear during childhood. Clinical spectrum is wide, ranging from fatal neonatal disease to asymptomatic individuals. Patients do not have to have clinical crises in order to have neurological or other organ compromise.
Natural history without treatment	Variable depending on the enzyme defect and the patient. Some will die as a neonate, others will survive with deficits and a few others will remain asymptomatic.
Natural history with treatment	About 60% of patients die within the first year of life and of those that survive, 40% are distinctly developmentally impaired. Age of onset of symptoms can help prognosticate – those with later onset tend to have a more benign course. Liver and liver/kidney transplant are one treatment option. However, liver transplants have significant preoperative risk and there is documentation of neurological problems after transplant despite improved biochemical values. Renal transplants have shown good response with drops in methylmalonic acid levels, normalization of the diet and absence of acute episodes of metabolic decompensation. However, the effect of any type of transplant is limited because the MMA enzyme is in all tissues and the transplants do not affect the levels made in the cerebrospinal fluid and brain.
Treatment	Protein restricted diet, hydroxy-cobalamine injections, carnitine supplementation and oral antibiotic therapy to decrease gut production of propionate. Special medical foods (formula) deficient in methionine, threonine, valine, isoleucine, odd chain fatty acids and cholesterol. Liver transplant and liver/kidney transplant.
Other	N/A
Physical phenotype	Most patients have no obvious dysmorphic features. Some patients, in whom there is known consanguinity, have had associated birth defects, congenital heart defects, hydronephrosis and facial dysmorphisms.
Inheritance	Autosomal recessive
General population incidence	1:48,000
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	Liver, kidneys, cerebrospinal fluid, brain
Enzyme Function	Catalyzes methylmalonyl-CoA to succinyl-CoA
Missing Enzyme	Methylmalonyl-CoA mutase
Metabolite changes	Increased methylmalonic acid in blood and urine.
Gene	MCM
Gene location	6p12-q21.2
DNA testing available	Sequencing available internationally
DNA testing detail	N/A
Prenatal testing	Possible via enzyme assay on amniocytes or CVS.
MS/MS Profile	Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine.
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=251000
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Multiple Carboxylase Deficiency

Alternate name(s)	Holocarboxylase Synthetase Deficiency; Holocarboxylase Deficiency Neonatal Form)
Acronym	MCD
Disease Classification	Organic Acid Disorder
Variants	Neonatal Form
Variant name	Multiple Carboxylase Deficiency, Neonatal Form
Symptom onset	Anytime from birth to 15 months of age.
Symptoms	Infants generally present with food refusal, vomiting, breathing problems, hypotonia, seizures, and lethargy. Severe metabolic/lactic acidosis, organic aciduria, mild hyperammonemia and variable hypoglycemia can lead to coma and death if not treated. Survivors can have neurological damage. Patients may have skin rash and alopecia at later stages.
Natural history without treatment	Repeated bouts of acidosis, skin rashes, failure to thrive, coma, developmental delay and death.
Natural history with treatment	Children with holocarboxylase synthetase deficiency, treated with biotin have normal growth and development. However, some only partly respond to therapy and one has been reported to be unresponsive to biotin therapy.
Treatment	Majority of cases respond readily to biotin supplementation. Biotin increases the functional activation of the carboxylase enzymes.
Physical phenotype	None
Inheritance	Autosomal recessive
General population incidence	1:87,000
Ethnic differences	No known population at increased risk
Missing Enzyme	Holocarboxylase synthetase (HS) attaches biotin to the four carboxylase enzymes (pyruvate carboxylase; priopionyl CoA carboxylase; beta-methylcrotonyl CoA carboxylase; acetyl CoA carboxylase) in order to activate them. Deficiency of HS results in functional deficiencies of all the carboxylase enzymes.
Gene	HLCS
Gene location	21q22.1
MS/MS Profile	C3 (propionyl carnitine) – elevated C5-OH (3-hydroxyisovaleryl carnitine) - elevated
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=210200
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Phenylketonuria

Alternate name(s)	Hyperphenylalaninemia, Phenylalanine hydroxylase deficiency, Følling disease
Acronym	PKU
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Benign phenylketonuria, Mild phenylketonuria, Variant phenylketonuria, Biopterin-responsive phenylketonuria Tetrahydrobiopterin deficiencies: GTP cyclohydrolase I deficiency, 6-Pyruvoyl-tetrahydropterin synthase deficiency, Dihydropteridine reductase deficiency, Pterin-4_-carbinolamine dehydratase deficiency
Symptom onset	Infancy
Symptoms	Mental retardation, decreased pigmentation relative to family members, eczematous rash, seizures, abnormal gait, and unusual “mousy” odor to urine.
Natural history without treatment	Mental retardation in the moderate to severe range, hyperactivity, eczema, mild neurologic manifestations, possible abnormal gait, microcephaly.
Natural history with treatment	If diet instituted early, normal IQ and development can be expected.
Treatment	Dietary restriction of phenylalanine with supplementary formula for tyrosine and essential amino acids.
Other	“Mousy” or “musky” smelling urine. Females with PKU are at-risk to have children affected by maternal PKU (increased levels of phenylalanine are teratogenic).
Physical phenotype	No abnormalities present at birth. May develop widely-spaced incisors, pes planus, epicanthus and microcephaly.
Inheritance	Autosomal recessive
General population incidence	1:10,000
Ethnic differences	Yes
Population	Turks, Irish
Ethnic incidence	Turks (1:2600), Irish (1:4500)
Enzyme location	Liver
Enzyme Function	Converts phenylalanine to tyrosine
Missing Enzyme	Phenylalanine hydroxylase
Metabolite changes	Increased plasma phenylalanine, increased phenylpyruvic acid in urine, decreased plasma tyrosine.
Gene	PAH (E.C 1.14.16.1)
Gene location	12q24.1
DNA testing available	Yes
DNA testing detail	Direct and linkage testing available. Over 380 mutations have been identified in PAH gene and direct DNA testing is available on limited clinical basis.
Prenatal testing	DNA testing is possible if mutations known. RFLP analysis is successful in 75% of families.
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=261600
Genetests Link	www.geneclinics.org
Support Group	National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Propionic acidemia

Alternate name(s)	Propionyl-CoA carboxylase deficiency, PCC deficiency, Ketotic hyperglycinemia
Acronym	PA
Disease Classification	Organic Acid Disorder
Variants	Yes
Variant name	Late onset (> 6weeks)
Symptom onset	Neonatal
Symptoms	Episodic crises leading to neurologic damage, coma and death.
Natural history without treatment	Metabolic crises may lead to neurologic damage including mental retardation, movement disorders, seizures, coma and sudden death are also possible.
Natural history with treatment	If treatment instituted before metabolic crisis, normal IQ and development may be seen. Treatment may improve some symptoms of affected individuals.
Treatment	Protein restricted diet with supplementary medical formula, carnitine supplementation, ketone monitoring, avoidance of fasting, cornstarch supplementation, biotin supplementation. Antibiotic (metronidazole and neomycin) treatment. Human growth hormone therapy.
Other	N/A
Physical phenotype	Characteristic facies including frontal bossing, widened depressed nasal bridge, epicanthal folds, long philtrum, upturned curvature of the lips and possible hypoplastic/inverted nipples.
Inheritance	Autosomal recessive
General population incidence	1:35,000 to 1:75,000 (may be underestimate as infants may die undiagnosed)
Ethnic differences	Yes
Population	Saudi Arabia
Ethnic incidence	1:2000 to 1:5000
Enzyme location	Mitochondria
Enzyme Function	Intermediary in the metabolism of isoleucine, valine, threonine and methionine.
Missing Enzyme	Propionyl-CoA carboxylyase
Metabolite changes	Increased glycine in blood and urine, 3-hydroxypropionic acid in blood and urine, methylcitrate, tiglic acid, tiglylglycine butanone and propionyl glycine in urine.
Gene	Enzyme is made up of alpha and beta subunits coded for by different genes - PCCA and PCCB.
Gene location	PCCA = 13q32 PCCB = 3q13.3-22
DNA testing available	Not available on a routine basis, but may be available on a research basis.
DNA testing detail	No common mutations known.
Prenatal testing	Enzyme activity in amniocytes. GCMS assay in amniotic fluid. If DNA mutations known, DNA testing is possible.
MS/MS Profile	N/A
OMIM Link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=232000
Genetests Link	www.genetests.org
Support Group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Short-chain acyl-CoA dehydrogenase deficiency

Acronym	SCADD or SCAD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	Late-onset with chronic myopathy
Symptom onset	Neonatal - but very variable; may be asymptomatic.
Symptoms	Neonatal - failure to thrive, hypotonia, metabolic acidosis, seizures and developmental delay.
Natural history	Developmental delay, hypotonia and muscle weakness have been observed without treatment, but the vast majority of patients detected via MS/MS newborn screening have been entirely asymptomatic.
Natural history with treatment	The efficacy of treatment is unknown.
Treatment	Carnitine supplementation, restriction of dietary fat. A few patients have shown improvements on riboflavin supplements.
Other	Acute fatty liver of pregnancy and HELLP syndrome have been reported as maternal complications in pregnancy, but may be coincidental.
Physical phenotype	None reported
Inheritance	Autosomal recessive
General population incidence	1:40,000 – 1:100,000
Ethnic differences	None
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondrial matrix in liver, muscle, fibroblasts
Enzyme Function	
Missing Enzyme	Short-chain acyl-CoA dehydrogenase
Metabolite changes	Ethymalonic acid in urine, methylsuccinate and butyrylglycines in urine.
Gene	ACADS
Gene location	12g22-qter
DNA testing available	Yes - but interpretation of results is difficult.
DNA testing detail	Limited mutational hotspots and common susceptibility alleles
Prenatal testing	Enzymatic
MS/MS Profile	Elevated C4 Cbutyrylcarnitine
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=606885
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Organic Acidemia Association http://www.ooanews.org Save Babies through Screening Foundation http://savebabies.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name	**Sickle Cell Disease**
Alternate Name(s)	Sickle Cell Anemia
Acronym	Hb S/S
Disease Classification	Hemoglobinopathy
Symptom onset	May be asymptomatic.
Symptoms	Any sign of illness in an infant with sickling disease is a potential medical emergency. Acute and chronic tissue injury can occur when sickled cells cause vascular occlusion. Sickling diseases can cause severe pain anywhere in the body, but most often in the hands, arms, chest, legs and feet. Complications may include, but are not limited to, the following: sepsis, acute chest syndrome, hand-and-foot syndrome, splenic sequestration crisis, aplastic crisis, stroke and painful episodes.
Natural history without treatment	Infants with sickle cell disease are vulnerable to serious bacterial infections that can be life threatening.
Natural history with treatment	Reduced mortality and morbidity with penicillin prophylaxis.
Treatment	The National Institutes of Health clinical guidelines for management of sickle cell disease state, "Penicillin prophylaxis should begin by 2 months of age for infants with suspected sickle cell anemia, whether or not the definitive diagnosis has been established." Antibiotic therapy should continue until at least 5 years of age.
Inheritance	Autosomal recessive
General population incidence	1:500 for African American and Hispanic American.
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=603903
Genetests Link	www.geneclinics.org
Support Group	Sickle Cell Information Center http://www.scinfo.org/ Sickle Cell Disease Association of America, Inc. http://www.sicklecelldisease.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Trifunctional protein deficiency

Alternate name(s)	N/A
Acronym	LCHADD. LCHAD or TFP
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	Mitochondrial trifunctional protein deficiency
Symptom onset	Neonatal, infancy
Symptoms	Hypoketotic hypoglycemia, hypotonia, cardiomyopathy, hepatic disease, peripheral neuropathy and pigmentary retinopathy, rhabdomyolysis, sudden death
Natural history without treatment	Possible developmental delay due to damage from hypoglycemic episodes, possible death due to cardiomyopathy or hepatic failure.
Natural history with treatment	Intelligence is usually normal if there is no damage due to hypoglycemic crisis. Peripheral neuropathy, if present, may not improve with treatment.
Treatment	Avoidance of fasting, use of uncooked starch, MCT treatments, carnitine supplementation, DHA supplementation (may prevent retinopathy, but this has not been proven)
Other	Maternal complications in pregnancy include acute fatty liver of pregnancy, HELLP syndrome, and pre-eclampsia
Physical phenotype	Hypotonia, cardiomyopathy and possible retinal changes
Inheritance	Autosomal recessive
General population incidence	Rare
Ethnic differences	Yes
Population	Finnish
Ethnic incidence	1:240 carrier rate for common mutation G1528C in Finland
Enzyme location	Inner mitochondrial membrane, liver, heart, fibroblasts
Enzyme Function	Metabolizes long chain fatty acids (C-12 to C-16 in length)
Missing Enzyme	Long-chain 3-hydroxyacyl-CoA dehydrogenase or mitochondrial trifunctional protein
Metabolite changes	Increased 3-hydroxydicarboxylic acids in urine, increased saturated and unsaturated 3-hydroxy organic acids, possible elevated CPK during acute illness.
Gene	HADHA and HADHB (alpha and beta subunits)
Gene location	2p23
DNA testing available	Yes – mutation analysis
DNA testing detail	Common mutation, G1528C, accounts for 87% of all mutant alleles in LCHAD deficiency; 70% of affected individuals will be homozygous for this mutation. There is no common mutation in trifunctional protein deficiency.
Prenatal testing	Enzyme analysis, protein analysis and direct DNA (when applicable).
MS/MS Profile	C18:OH, C16:1OH, C16OH
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=600890
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Tyrosinemia, type 1

Alternate name(s)	Hereditary infantile tyrosinemia, Hepatorenal tyrosinemia, Fumarylacetoacetase deficiency, Fumarylacetoacetate hydrolase
Acronym	FAH deficiency
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Tyrosinemia I chronic-type, Tyrosinemia II, Tyrosinemia III
Symptom onset	Infancy
Symptoms	Hepatocellular degeneration leading to acute hepatic failure or chronic cirrhosis and hepatocellular carcinoma, renal Fanconi syndrome, peripheral neuropathy, seizures and possible cardiomyopathy.
Natural history without treatment	Chronic liver disease leading to cirrhosis and hepatocellular carcinoma. Renal tubular disease (Fanconi syndrome) with phosphaturia, aminoaciduria and often glycosuria. May lead to clinical rickets. Peripheral neuropathy. Self-injurious behavior, seizures and cardiomyopathy have been observed. Coagulation problems.
Natural history with treatment	Hepatitic disease may progress despite dietary treatment. NTBC treatment leads to improvements in kidney, liver and neurologic function, but may not affect incidence of liver cancer.
Treatment	Dietary restriction of phenylalanine and tyrosine. NTBC (2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanedione) treatment which improves hepatic and renal function. Liver transplantation when indicated to prevent hepatocellular carcinoma. Vitamin D to heal rickets.
Other	Unpleasant odor due to accumulation of methionine. Sometimes described as “cabbage-like” odor.
Physical phenotype	No abnormalities present at birth. May develop widely-spaced incisors, pes planus, epicanthus and microcephaly.
Inheritance	Autosomal recessive
General population incidence	1:100,000
Ethnic differences	Yes
Population	French Canadian (Saquency-Lac Saint Jean region) 1:20 carrier rate
Ethnic incidence	1:1846
Enzyme location	Liver, kidney, lymphocytes, fibroblasts
Enzyme Function	Metabolizes fumarylacetoacetic acid into fumaric acid and acetoacetic acid
Missing Enzyme	Fumarylacetoacetate hydrolase
Metabolite changes	Increased urinary succinylacetone, increased tyrosine and methionine in serum, increased alpha fetoprotein.
Gene	FAH
Gene location	15q23-25
DNA testing available	Yes
DNA testing detail	DNA for isolated populations
Prenatal testing	Enzymatic assay of amniocytes or CVS cells. Direct DNA testing in amniocytes or CVS cells if mutations known. Succinylacetone in amniotic fluid.
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=276700
Genetests Link	www.genetests.org
Support Group	National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

HEALTH CARE PROVIDER FACT SHEETS

Disease Name — Very long-chain acyl-CoA dehydrogenase deficiency

Alternate name(s)	N/A
Acronym	VLCADD
Disease Classification	Fatty Acid Oxidation Disorder
Variants	Yes
Variant name	With and without cardiomyopathy
Symptom onset	Primarily neonatal but some variability.
Symptoms	Hypoketotic hypoglycemia, hepatomegaly, myopathy, cardiomyopathy, adult-onset myopathy.
Natural history without treatment	Sudden infant death due to cardiac abnormalities is common.
Natural history with treatment	Diagnosis and treatment seem to decrease risk for sudden death.
Treatment	Avoidance of fasting, high carbohydrate, low-fat diet supplemented with MCT oil, IV glucose during illness, cornstarch supplementation, avoidance of long chain fatty acids, possible carnitine supplementation.
Other	May have history of a sibling dying of SIDS.
Physical phenotype	No particular dysmorphisms. Cardiomyopathy in infants.
Inheritance	Autosomal recessive
General population incidence	Rare – exact incidence not known
Ethnic differences	None reported
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondrial matrix, heart, liver
Enzyme Function	Long chain fatty acid beta-oxidation
Missing Enzyme	Very long-chain acyl-CoA dehydrogenase
Metabolite changes	Dicarboxylic aciduria, decreased urinary carnitine at times of illness, plasma free carnitine - normal to low, increased plasma long-chain acylcarnitines mildly increased ammonia, lactate and creatine kinase.
Gene	ACADVL
Gene location	17p11.2-p11.1
DNA testing available	Available on a research basis
DNA testing detail	No common mutations have been found. If a mutation in a proband is detected, DNA carrier screening is possible.
Prenatal testing	Enzyme and protein analysis. If a mutation in a proband is detected, DNA prenatal diagnosis via CVS or amniocytes is possible.
MS/MS Profile	Elevated C16:1, C14:2, C14:1, C18:1
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=201475
Genetests Link	www.genetests.org
Support Group	FOD Family Support Group http://www.fodsupport.org Save Babies through Screening Foundation http://www.savebabies.org Genetic Alliance http://www.geneticalliance.org

Parent Fact Sheets

PARENT FACT SHEET

DISORDER

3-methylcrotonyl CoA carboxylase deficiency (3MCC)

CAUSE

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them. 3MCC deficiency occurs when an enzyme is missing or not working properly.

IF NOT TREATED

Each child with 3MCC deficiency may have somewhat different effects. Babies with 3MCC deficiency are healthy at birth. If symptoms occur, they often start after 3 months of age. Some babies do not have symptoms until 6 months to 3 years of age. If not treated these babies could go into metabolic crisis which could lead to seizures, breathing problems, liver failure, coma or death.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is needed throughout the child's life.

- A food plan low in leucine with limited amounts of protein is sometimes needed. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables).
- Medical foods and formula: special low-protein flours, pastas and rice that are made especially for people with organic acid disorders.
- Some children may benefit by taking a medication called L-carnitine.

IF TREATED

With prompt and careful treatment, children who have shown symptoms of 3MCC deficiency have a good chance to live healthy lives with typical growth and development. Even with treatment, some children still have repeated bouts of metabolic crisis that require close monitoring throughout their life.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Argininosuccinic Acidemia (ASA)

CAUSE

ASA occurs when an enzyme called argininosuccinic acid lyase is either missing or not working properly. This enzyme's job is to help remove ammonia from the body. When the ASA lyase enzyme is not working, ammonia and other harmful substances build up in the blood.

IF NOT TREATED

Normally, the body changes ammonia into a substance called "urea." Urea is then safely removed from the body in the form of urine. If urea is not removed from the body, it begins to build up in the blood and causes brain damage. In the most common form of ASA, infants are generally healthy at birth but usually develop symptoms within a few days of life. Without treatment, many babies die within the first few weeks of life. There is also a second form of ASA in which very mild symptoms start in late infancy or early childhood.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is needed throughout the child's life.

- Most children need to eat a diet made up of very low-protein foods, special medical foods, and sometimes a special formula. The dietician will develop a plan for you to follow.
- Most children with ASA are given arginine supplements. Arginine helps the body remove ammonia from the blood. Your child's metabolic specialist will determine the best treatment available. Arginine is available by prescription only.
- Your child will require frequent blood tests to monitor amino acid and ammonia levels in the blood. Diet and medication may require adjustments based on these lab results.
- Contact your child's doctor immediately at the start of any illness. Children with ASA may need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and lifelong treatment, children with ASA may be able to live healthy lives with typical growth and learning. Early treatment can lessen the risk for brain damage and mental retardation by preventing high ammonia levels. Even with treatment, some children still have episodes of high ammonia. This can result in brain damage and can cause lifelong learning problems, mental retardation, and spasticity (spasms of the muscles and tendons).

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Beta ketothiolase deficiency (BKT)

CAUSE

BKT occurs when the mitochondrial acetoacetyl-CoA thiolase enzyme (MAT) is either missing or not working properly. This enzyme's job is to help break down the amino acid called isoleucine. Isoleucine is found in all foods that contain protein. When a child with BKT eats food containing isoleucine, harmful substances called organic acids build up in the blood and urine, causing metabolic crisis and brain damage.

IF NOT TREATED

Each child with BKT has slightly different effects. The first symptoms often start around age one, although babies can have symptoms earlier or later than this. BKT causes episodes of illness called metabolic crises, which can cause brain damage, learning disabilities, mental retardation, and other problems.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment should begin immediately and will continue throughout life.

- Your child needs to avoid going a long time without food. This is to avoid a metabolic crisis. Children with BKT should not go more than 4 to 6 hours without food and some may require more frequent feedings. Your child's metabolic specialist will advise you as to whether your child needs to eat more often than usual and how to space your child's meals.
- The dietician will help develop a food plan that meets your child's needs. Any changes in diet should only be made by the dietician. While some children with BKT can eat normal amounts of protein, others will need to be on a low-protein diet.
- Periodic urine tests should be done to test the level of ketones. This can be done at home or at the doctor's office. Ketones are substances formed when body fat is broken down to use for energy. This happens after going without food for long periods of time, during illness, or during periods of heavy exercise. Ketones in the urine may signal the start of a metabolic crisis.
- Contact your child's doctor immediately at the start of any illness. Children with BKT may require hospitalization to prevent metabolic crisis.

IF TREATED

If treatment is started early and metabolic crises do not occur, your child is likely to have normal growth and intelligence. Even with treatment, some children still have repeated episodes of metabolic crises, which can cause brain damage resulting in learning difficulties, mental retardation and other problems.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Biotinidase Deficiency (BTD)

CAUSE

BTD affects the way a person's body uses the vitamin, biotin. Biotin is an important vitamin that helps enzymes, called carboxylases, make certain fats and carbohydrates and help break down proteins. A child with BTD cannot use biotin when it is still bound to food. Biotin can only be used in its free form and is essential for proper growth and development.

IF NOT TREATED

Most infants with BTD appear normal at birth, but develop serious symptoms after the first few weeks or months of life. Low biotin levels can cause seizures, developmental delay, hearing loss, vision problems, and other serious and sometimes life-threatening illnesses.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist. Treatment is needed throughout life.

- Biotin supplements can be taken orally and come in many forms – capsules, tablets, and liquids. Biotin supplements are safe and non-toxic.
- Your child's metabolic specialist will determine the proper dose that should be taken.
- A prescription is required for biotin supplements.
- Regular blood work will be required to monitor your child's progress in the event any changes in treatment need to be made.

IF TREATED

Because newborn screening can detect virtually all cases of BTD, treatment can be started very quickly. If your child begins treatment before showing any symptoms, biotin supplements can prevent all symptoms from occurring. If your child is already showing symptoms, most of those symptoms will improve upon being treated. Biotin therapy will not reverse brain damage that occurs before treatment is started, but it will prevent further damage from occurring. However, vision and hearing loss may not respond to biotin treatment, depending on the time between the beginning of symptoms and the start of treatment. Some children achieve rapid developmental milestones while others show continued developmental delays.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Carnitine uptake defect (CUD)

CAUSE

CUD occurs when an enzyme, called "carnitine transporter" (CT), is either missing or not working properly. This enzyme's job is to carry a substance called carnitine into our cells. Carnitine helps the body make energy from the fat in food and also helps us use fat already stored in the body. When the normal CT enzyme is not functioning properly, the body must rely solely on glucose. There is a limited supply of glucose in our bodies and once it is used up, the body tries to use fat without success. This leads to low blood sugar, called hypoglycemia, and the build up of harmful substances in the blood. This is referred to as a metabolic crisis.

IF NOT TREATED

There are two main forms of CUD: one begins in infancy and the other in childhood. Babies with CUD usually begin showing symptoms between birth and three years old. Metabolic crisis often occurs when a child has not eaten for more than a few hours, gets sick, or develops an infection. Repeated episodes of metabolic crisis can cause brain damage and result in learning problems or mental retardation.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed throughout life.

- Your child needs to avoid going a long time without food. This is to avoid a metabolic crisis. These children should not go more than 4 to 6 hours without food and some may require more frequent feedings. It is important that these children be fed in the night – meaning you will need to wake them up to eat if they do not wake up on their own – and even if they are not hungry.
- The dietician will develop a diet for your child that contains low amounts of fat and a high amount of carbohydrates. Your child's diet should never be changed without the approval of your dietician.
- The main treatment for CUD is a supplement of L-carnitine. This is a safe and natural substance that helps body cells make energy. It also helps the body get rid of harmful wastes. L-carnitine can reverse the heart problems and muscle weakness that occur in children with CUD.
- Your metabolic specialist must prescribe the L-carnitine supplement and instruct you on the recommended dose.
- Contact your child's doctor immediately at the start of any illness. Children with CUD need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and careful treatment, children with CUD usually live healthy lives with typical growth and development. Infants with CUD who have repeated episodes of metabolic crisis may have permanent brain damage. This can cause learning disabilities or mental retardation.

12/1/05 Update -8J-

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Citrullinemia (CIT)

CAUSE

CIT occurs when an enzyme called "argininosuccinic acid synthetase" (ASAS), is either missing or not working properly. This enzyme's job is to help break down certain amino acids and to remove ammonia from the body. When the enzyme is not working, an amino acid called citrulline builds up in the blood. Ammonia and other harmful substances also build up. This causes brain damage and, if not treated, can cause death.

IF NOT TREATED

Normally, the body changes ammonia into a substance called "urea." Urea is then safely removed from the body in the form of urine. If urea is not removed from the body, it begins to build up in the blood and causes brain damage. In the most common form of CIT, infants may seem healthy at birth but develop symptoms within the first few days of life. There is also a milder form of CIT in which symptoms start in late infancy or early childhood. Without treatment, most babies die within the first few weeks of life.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed throughout life.

- Most children need to eat a diet made up of very low-protein foods, special medical foods, and sometimes a special formula. The dietician will develop a plan for you to follow.
- Most children with CIT are given arginine supplements. Arginine helps the body remove ammonia from the blood. Your child's metabolic specialist will determine the best treatment available. Arginine is available by prescription only.
- Your child will require frequent blood tests to monitor amino acid and ammonia levels in the blood. Diet and medication may require adjustments based on these lab results.
- Contact your child's doctor immediately at the start of any illness. Children with CIT may need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and lifelong treatment, children with CIT may be able to live healthy lives with typical growth and learning. Early treatment can lessen the risk for brain damage and mental retardation by preventing high ammonia levels. Even with treatment, some children still have episodes of high ammonia. This can result in brain damage and can cause lifelong learning problems, mental retardation, and spasticity (spasms of the muscles and tendons).

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Congenital Adrenal Hyperplasia (CAH)

CAUSE

In CAH, the child is born with overgrown adrenal glands, which are unable to make enough cortisol. Cortisol is essential for life, as it is needed to maintain an adequate energy supply and blood sugar level. Cortisol is also called a "stress hormone" because our adrenal glands make more of it when we are under physical or emotional stress to protect our bodies from illness or injury. Another important hormone made by the adrenal gland is called aldosterone, a salt-retaining hormone. Aldosterone is used by the kidney to help the body maintain normal levels of sodium and potassium, which are necessary for all cells to work normally. Without adequate levels of these minerals in the body, too much salt and water are lost in the urine, leading to salt deficiency and dehydration. Children with CAH also produce too much androgen (male hormone). The overproduction of male hormone in female infants will cause the external genitals to take on a male appearance, although the internal parts may be quite normal. For this reason, females are more likely to be diagnosed earlier than boys. Boys are likely to be diagnosed as a result of entering puberty at an extremely early age (some as young as 2-3 years old) and appearing to be very tall for their age.

IF NOT TREATED

Untreated CAH can result in serious illness due to salt-wasting and, in some cases, death. It may be difficult to tell if the CAH child's genitals are male or female. Without treatment, the clitoris in the female infant will continue to enlarge into a male-like penile structure. Untreated females do not have normal periods and are unable to have children as an adult. The testicles of a boy with CAH cannot function well and will not make sperm normally. High levels of androgens cause rapid early physical growth that will also stop prematurely, resulting in the child becoming a very short adult.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist. CAH cannot be "outgrown" and treatment will be needed throughout life.

- CAH is treated with hormone-replacement medications. The metabolic specialist will determine the proper amount your child should take each day. These medications will require a prescription.
- Reconstructive surgery may be required for girls with masculine external genitalia and can be performed as early as one to three months of age.
- Blood tests will need to be performed frequently to monitor hormone levels and adjust medications as necessary.
- Contact your child's doctor immediately at the start of any illness. Children with CAH may need to be treated at a hospital to prevent serious health problems.

IF TREATED

With regular medication, your child with CAH can lead a normal life. There are no known mental delays associated with CAH. Life expectancy is normal. Women with CAH that take their medications as directed have no difficulties becoming pregnant and carrying a baby to term. Men who take their medications appropriately also have normal fertility.

12/1/05 Update -8N-

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Congenital Hypothyroidism (CH)

CAUSE

The thyroid gland is responsible for producing the hormone, thyroxine (T4). Thyroxine is very important in the growth and development of the infant's brain, body, bone development, in regulating the infant's body temperature, and in making sure that fat and muscle are distributed normally throughout the body. Under normal circumstances, the thyroid gland is regulated by the pituitary gland. The pituitary gland recognizes when the body is not producing enough T4 and produces thyroid stimulating hormone (TSH). There are a variety of causes for CH. The thyroid gland may never have developed. The thyroid gland may have developed abnormally or be smaller than normal. The thyroid could even be misplaced to an abnormal location.

IF NOT TREATED

There is a high rate of severe mental retardation and growth delays in untreated children with CH or in those children who were delayed in beginning treatment.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist. Treatment is needed throughout life.

- Your child will require thyroid replacement medications. The metabolic specialist will prescribe these medications and make adjustments in the dosage as necessary.
- Remember to never mix thyroid medications with soy formula as the baby will be unable to absorb the medication and will not receive the medication's benefits.

IF TREATED

Children that are treated within the first month to six weeks of life can prevent mental retardation, even to the point of having no mental or physical delays, allowing them to lead normal lives. Treatment that begins after 4-6 weeks of life may not reverse any mental impairments that have already occurred, but it can reverse physical impairments that have already occurred.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Cystic Fibrosis (CF)

CAUSE

CF is an inherited disease that causes the exocrine glands to not work properly. The exocrine glands normally make thin, slippery secretions like sweat, mucus, tears, saliva, and digestive juices. In CF, the exocrine glands make thick, sticky mucus that may plug passageways (ducts) to the lungs, intestines, and other organs. Children with CF also have a high amount of salt and potassium in their sweat, which may cause problems during times of increased sweating. CF is not contagious and does not affect the brain. Most infants with CF are diagnosed within the first three years of life. As adults, the reproductive system will also be affected by CF. The thick mucus blocks the passageway for men to pass sperm and, in women with CF, blocks sperm from reaching the egg. Approximately 98 percent of men with CF are unable to father a child. Women with CF may have greater difficulty getting pregnant than women without CF.

IF NOT TREATED

The thick mucus caused by CF can clog the child's airway and make it difficult to breathe. It can also cause frequent lung infections. Because of the high amount of minerals lost during sweating, it is very easy for a child with CF to become dehydrated when they become overheated. The thick mucus caused by CF also keeps food from being properly digested, resulting in poor growth and malnutrition or a blockage in the intestine that requires medical treatment. Any of these events, in an untreated child with CF, are potentially life-threatening.

TREATMENT OPTIONS

Your child will need to be under the care of a cystic fibrosis specialist and a dietician. Treatment is required throughout life.

- The child with CF will need to take pancreatic enzymes to help with digestion. They may also have to take numerous other medications every day. These will be prescribed by their cystic fibrosis specialist.
- Daily lung percussion (clapping the hand on the child's chest and back) is often required for the CF child. This can be done in your home and usually lasts for 30 minutes each session, twice a day. The CF specialist will train you on the proper way to do this.
- Your child will also require daily respiratory medications that may be given in a pill, as a vapor (by being inhaled), or through the vein. This helps thin the mucus in the lungs and prevents lung infections from occurring.
- There should be absolutely no cigarette smoking around a child with CF!!!!!
- Contact your child's doctor immediately at the start of any illness. Children with CF may need to be treated in a hospital when ill to prevent serious health problems.

IF TREATED

With treatment, children with CF are seeing an increased life expectancy and are living active lives.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Galactosemia (GALT)

CAUSE

GALT is caused when the liver enzyme that helps the body break down galactose (a form of milk sugar) is either missing or not working properly. Since galactose cannot be broken down in a child with GALT, it builds up in the body and causes damage to the liver, brain, kidneys, eyes, and various other body systems.

IF NOT TREATED

Babies with GALT may appear normal at birth, but their condition can rapidly worsen if they are given any form of human or animal milk products. Exposure to milk products may result in liver damage, mental retardation, cataract formation, partial blindness, and kidney failure – to the point where death can occur as early as one to two weeks of age.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment will be needed throughout life.

- Your child's metabolic specialist and dietician will put your child on a soy-based formula and develop a diet plan, as your child gets older.
- As the patient with GALT must avoid any food that contains milk or milk products, you will have to learn to read product ingredient labels at the grocery in order to also avoid foods that may contain dry milk products, as well.

IF TREATED

If diagnosis is made early and milk products are strictly avoided, the child with GALT can expect to live a relatively normal life. However, mild mental delays may still develop in GALT patients despite strict avoidance of galactose.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Glutaric acidemia type 1 (GA-1)

CAUSE

GA-1 occurs when an enzyme called "glutaryl-CoA dehydrogenase" is either missing or not working properly. This enzyme's job is to break down a substance called glutaric acid. Glutaric acid is made when the amino acids lysine, hydroxylysine, and tryptophan are processed by the body. Whenever a child with GA-1 eats a food containing lysine or tryptophan, glutaric acid and other harmful substances build up in the blood. Lysine and tryptophan are found in all foods that contain protein.

IF NOT TREATED

Babies with GA-1 are usually healthy at birth, although many are born with a larger-than-average head size. Other symptoms usually start between two months and four years of age. GA-1 causes episodes of severe illness called metabolic crises. A metabolic crisis can cause brain damage and problems with involuntary movements of the muscles and tendons (this is called spasticity).

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is needed throughout life.

- Your child's dietician will develop a food plan made up of foods low in lysine and tryptophan. A special formula will need to be given to your child as an infant. Special medical foods will also be part of this food plan.
- No changes to your child's diet should occur without permission and supervision of the dietician.
- Riboflavin is a vitamin that helps the body use protein. It may also help remove glutaric acid from the blood. Your child's metabolic specialist will prescribe the proper dose and make any changes when necessary.
- Some children may be helped by taking L-carnitine. This is a safe and natural substance that helps the body make energy. It also helps the body get rid of harmful wastes. Your metabolic specialist will prescribe this medication, if necessary.
- Your child will have regular blood tests to measure their amino acid levels. Urine tests may also need to be done. The results of these tests may result in medication or diet changes.
- Children with GA-1 need to eat more carbohydrates and drink more fluids when they are ill – even when they are not hungry. They also should avoid all protein when they are ill.
- Contact your child's doctor immediately at the start of any illness. Children with GA-1 may need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and lifelong treatment, children with GA-1 can often live healthy lives with typical growth and learning.

For more information go to the following website: http://www.newbornscreening.info

Parent Fact Sheet

DISORDER

Hemoglobin S-βeta Thalassemia disease (Hb S/β)

CAUSE

B (Beta) thalassemia is a type of inherited blood disorder that can cause anemia (a low number of red blood cells). It affects a person's ability to produce hemoglobin, the protein in red blood cells that delivers oxygen to all parts of the body.

Signs and symptoms of β (beta) thalassemia are severe in the form of the disorder known as thalassemia major and less severe in the form called thalassemia intermedia. Signs and symptoms of thalassemia major appear in the first 2 years of life. Infants become pale and listless, have a poor appetite, grow slowly, and often develop jaundice (yellowing of the skin). The spleen, liver, and heart may also be enlarged.

IF NOT TREATED

Most children with thalassemia major appear healthy at birth, but during the first year or two of life they become pale, listless and fussy, and have a poor appetite. They grow slowly and often develop jaundice (yellowing of the skin). Adolescents with the severe form may experience delayed puberty. Individuals with thalassemia intermedia may have no symptoms or mild symptoms through childhood and adolescence.

Without treatment, the spleen, liver, and heart soon become greatly enlarged. Bones become thin and brittle; face bones become distorted, and children with thalassemia often look alike. Heart failure and infection are the leading causes of death among children with untreated thalassemia major.

TREATMENT OPTIONS

- The use of frequent blood transfusions and antibiotics has improved the outlook for children with thalassemia major. When children with thalassemia major are treated with frequent transfusions (generally every 3 to 4 weeks) aimed at keeping their hemoglobin level near normal, many of the complications of thalassemia can be prevented. This form of treatment, referred to as "hypertransfusion," enhances the child's growth and well-being, and usually prevents heart failure and bone deformities.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

Children with thalassemia major who are treated with frequent blood transfusions and iron chelation live longer. Since intensive chelation treatment was introduced only in the 1960s, continuing studies may show that treated individuals are living even longer.

Thalassemia has been cured using bone marrow transplants. However, this form of treatment is possible only for a small minority of patients who have a suitable bone marrow donor, and the transplant procedure is still risky and can result in death.

For more information go to the following website: http://www.newbornscreening.info

Parent Fact Sheet

DISORDER

Hemoglobin S/C Disease (Hb S/C)

CAUSE

Sickle cell disease is an inherited blood disorder characterized by defective hemoglobin (a protein in red blood cells that carries oxygen to the tissues of the body).

Sickle cells only live for about 15 days, while normal hemoglobin can live up to 120 days. Also, sickle cells risk being destroyed by the spleen because of their shape and stiffness. The spleen is an organ that helps filter the blood of infections and sickled cells get stuck in this filter and die. Due to the decreased number of hemoglobin cells circulating in the body, a person with sickle cell disease is chronically anemic. The spleen also suffers damage from the sickled cells blocking healthy oxygen carrying cells. Without a normal functioning spleen, these individuals are more at risk for infections. Infants and young children are at risk for life-threatening infections.

Sickle cell - hemoglobin C disease - The child has both HbS and HbC. This is often referred to as HbSC. Hemoglobin C causes red blood cells, called target cells, to develop. Having just some hemoglobin C and normal hemoglobin, a person will not have any symptoms of anemia. However, if the sickle hemoglobin S is combined with the target cell, some mild to moderate anemia may occur. These children often suffer some of the complications associated with HbSS, sickle cell disease, but to a milder degree. Vasoocclusive crises (the flow of blood is blocked because the sickled cells have become stuck in the blood vessels), organ damage from repeated sickling and anemia, and high risk for infection are all similar traits for HbSS and HbSC.

TREATMENT OPTIONS

- Pain medications (for sickle cell crises).
- Drinking plenty of water daily (8 to 10 glasses) or receiving fluid intravenously (to prevent and treat pain crises).
- Blood transfusions (for anemia, and to prevent stroke; transfusions are also used to dilute the HbS with normal hemoglobin to treat chronic pain, acute chest syndrome, splenic sequestration and other emergencies.)
- Penicillin (to prevent infections).
- Folic acid (to help prevent severe anemia).
- Hydroxyurea (a medication recently developed that may help reduce the frequency of pain crises and acute chest syndrome; it may also help decrease the need for frequent blood transfusions. The long-term effects of the medication are unknown.)
- Bone marrow transplant (has been effective in curing some children with sickle cell disease; the decision to undergo this procedure is based on the severity of the disease and a suitable bone marrow donor. These decisions need to be discussed with your child's physician.)

IF TREATED

With early detection and comprehensive medical care, most people with sickle cell disease are in fairly good health most of the time. Most individuals can be expected to live well into adulthood, enjoying an improved quality of life including the ability to choose a variety of education, career, and family planning options for themselves.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Homocystinuria (HCY)

CAUSE

HCY occurs when an enzyme called "cystathionine beta-synthase" (CBS) is either missing or not working properly. This enzyme's job is to break down methionine, an amino acid. When the CBS enzyme is not working correctly, methionine and another amino acid, homocystine, build up in the blood and cause problems.

IF NOT TREATED

Babies with HCY look healthy and normal at birth. If the condition is not treated, HCY can cause growth and learning delays, which are usually noticed between one and three years of age. HCY can also affect the eyes, bones, heart, and blood vessels.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is needed throughout life.

- The infant with HCY will require a special formula, which will be prescribed by the metabolic specialist and dietician.
- As your child gets older, the dietician will develop a special food plan, which may include special medical foods.
- The metabolic specialist will prescribe medications for your child and the proper amounts to give. These will include Vitamin B6, Betaine, Vitamin B12, Folic Acid, and L-cystine.
- Do not make any changes to medications or diet without the approval and permission of the metabolic specialist and the dietician.
- Your child will require regular blood and urine tests to check their amino acid levels. Diet and medication changes may occur as a result.
- Contact your child's doctor immediately at the start of any illness. Children with HCY may need to be treated in a hospital to prevent serious health problems.

IF TREATED

With lifelong treatment, many children experience normal growth and learning abilities. Treatment may lower the risk of blood clots, heart disease and stroke. Treatment also decreases the chance of eye problems. Children who begin treatment later in life may have mental retardation and behavior problems.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Hydroxymethylglutaric Aciduria (3-OH 3 CH3 glutaric aciduria) (HMG)

CAUSE

HMG occurs when the HMG CoA lyase enzyme is missing or not working properly. This enzyme breaks down leucine, which is found in all foods that contain protein, and helps the body make ketones, used from fat stored in the body to produce energy. When a child is ill or goes without food too long, the body breaks down its own protein and fat to use for energy. Because of the deficient HMG CoA lyase enzyme, this can cause a metabolic crisis due to the HMG child's inability to process leucine and produce ketones.

IF NOT TREATED

HMG can exhibit different effects in each child. Babies with this condition are usually healthy at birth, although some show their first symptoms a few days after birth. Most babies, however, start to have symptoms between 3 months and 2 years of age. If not treated, many babies die during their first metabolic crisis. In surviving babies, repeated episodes of metabolic crisis can cause brain damage. This can result in life-long learning problems or mental retardation.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed throughout life.

- Your child needs to avoid going a long time without food. This is to avoid a metabolic crisis. These children should not go more than 4 to 6 hours without food and some may require more frequent feedings. It is important that these children be fed in the night – meaning you will need to wake them up to eat if they do not wake up on their own – and even if they are not hungry.
- A low-leucine diet with limited amounts of fat and protein and a high amount of carbohydrates is often recommended by the dietician in the form of special formula and foods.
- Some children may benefit from taking L-carnitine. This is a safe and natural substance that helps the body make energy. The metabolic specialist will decide if your child can benefit from this treatment. A prescription for this is required.
- Contact your child's doctor immediately at the start of any illness. Children with HMG need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and careful treatment, children with HMG lyase deficiency have a good chance to live healthy lives with typical growth and development. Even with treatment, some children still have repeated episodes of low-blood sugar and metabolic crisis. This can cause brain damage and may lead to life-long learning problems or mental retardation.

12/1/05 Update -8AD-

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Isovaleric Acidemia (IVA)

CAUSE

IVA occurs when an enzyme called "isovaleryl-CoA dehydrogenase" is either missing or not working properly. This enzyme's job is to help break down a harmful substance called isovaleric acid. It is made in the body when the amino acid, leucine, is broken down. When a child with IVA eats food containing leucine, isovaleric acid builds up in the blood and causes problems. Leucine is found in all foods that contain protein.

IF NOT TREATED

Infants with IVA seem healthy at birth. Often, the first symptoms start between one day and two weeks of age. IVA causes episodes of illness called metabolic crises. If not treated, many babies die during their first metabolic crisis. In those who survive, repeated episodes of metabolic crisis can cause brain damage. This can result in life-long learning problems or mental retardation.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed throughout life.

- The infant with IVA will require a special formula, which will be prescribed by the metabolic specialist and the dietician.
- As your child gets older, the dietician will develop a special food plan, which may include special medical foods.
- Glycine is an amino acid that helps the body get rid of isovaleric acid. It is often given as a supplement to children with IVA. It may help prevent metabolic crises. Your child's metabolic specialist will prescribe this supplement and the correct amount to take, if necessary.
- Some children may benefit by taking L-carnitine. This is a safe and natural substance that helps the body make energy. It also helps the body get rid of isovaleric acid and other harmful wastes. The metabolic specialist will decide whether or not your child needs L-carnitine and, if so, the proper amount they should take.
- Do not make any changes to medications or diet without the approval and permission of the metabolic specialist and the dietician.
- Contact your child's doctor immediately at the start of any illness. Children with IVA may need to be treated in a hospital to prevent serious health problems.

IF TREATED

With prompt and careful treatment, children with IVA have a good chance to live healthy lives with typical growth and development. However, even when treated, some children still have repeated occurrences of metabolic crisis, which can lead to life-long learning problems or mental retardation.

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Long Chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHAD)

CAUSE

People with LCHAD have problems breaking down fatty acids into energy for the body. LCHAD occurs when an enzyme called long chain 3-hydroxyacyl-CoA dehydrogenase is either missing or not working properly. When this enzyme is missing or not working properly the body cannot break down fat for energy so it relies on glucose, which the body only has limited amounts. Once the glucose is used up, the body tries to use fats without success. This leads to low blood sugar and the buildup of harmful substances in the blood.

IF NOT TREATED

The symptoms can vary from person to person. Hypoglycemia (low blood sugar) is usually the first symptom of a metabolic crisis. If the metabolic crisis is not treated, then the baby can have breathing problems, swelling of the brain, seizures and coma, sometimes leading to death.

If not treated the baby may have poor weight gain, delays in learning, delays in walking and other motor skills, enlarged liver, enlarged heart, vision loss, anemia, nerve problems and bouts of muscle weakness and pain.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child.
- Avoid hypoglycemia by having your baby eat at least every 4-6 hours; some babies may need to eat more often. It is important to feed them even during the night. They need to be woken up to eat if they do not wake up on their own.
- A diet high in carbohydrates and low in fat is recommended. Any diet changes should be made under the guidance of a dietician.
- MCT oil and L-Carnitine are often used as part of the food plan for people with LCHAD. Your metabolic doctor will guide you on how to use and will give you a prescription for these.
- Call your doctor at the start of any illness.
- Avoid prolonged exercise or exertion.

IF TREATED

Children who are treated early usually live healthy lives with typical growth and development. Some children continue to have episodes of hypoglycemia even with treatment. Some people still have vision, muscle, liver or heart problems even with treatment.

For more information go to the following website: http://www.newbornscreening.info

Parent Fact Sheet

Maple Syrup Urine Disease (MSUD)

CAUSE

MSUD stands for "maple syrup urine disease". It is named for the sweet maple syrup smell of the urine in untreated babies. This condition is one type of amino acid disorder. People with MSUD have problems breaking down certain amino acids found in protein.

Classic MSUD, the most common form, is caused by the absence of a group of enzymes called "branched-chain ketoacid dehydrogenase" (BCKAD). The job of this enzyme group is to break down three different amino acids called leucine, isoleucine and valine. When they cannot be broken down, these amino acids build up in the blood and cause problems.

Symptoms start as soon as a baby is fed protein, usually shortly after birth. Babies with MSUD have episodes of illness called metabolic crises. A metabolic crisis can cause severe health problems and, sometimes, even death.

IF NOT TREATED

The untreated child with MSUD can have repeated episodes of metabolic crisis. Symptoms of a metabolic crisis often occur after going too long without food, during illness or infection and during stressful events such as surgery.

Without treatment, brain damage can occur. This can cause mental retardation or spasticity. Some babies become blind. If not treated, most babies die within a few months.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child.
- In addition to a low-protein diet, children are often given a special medical formula as a substitute for milk. This formula gives them the nutrients and protein they need.
- Diet low in branched-chain amino acids (BCAA)-The diet is made up of foods that are very low in the BCAAs. This means your child will need to avoid foods such as cow's milk, regular formula, meat, fish, cheese and eggs. Regular flour, dried beans, nuts, and peanut butter also have BCAAs and must be avoided or strictly limited. Many vegetables and fruits have only small amounts of the BCAAs and can be eaten in carefully measured amounts.
- Your child will have regular blood tests to measure amino acid levels. The diet and formula may need to be adjusted based on blood test results.
- Children with a rare form of MSUD, called "thiamine-responsive MSUD", can often be helped by thiamine supplements. Do not use any supplements without checking with your doctor.
- Call your doctor at the start of any illness. For children with MSUD, even minor illness can cause a metabolic crisis.

IF TREATED

With prompt and lifelong treatment, children with MSUD often have healthy lives with typical growth and development. Early treatment can help prevent brain damage and mental retardation. Even with treatment, some children still develop swelling of the brain or have episodes of metabolic crisis. Children who have repeated metabolic crises may develop permanent brain damage. This can cause lifelong learning problems, mental retardation or spasticity.

12/1/05 Update -8AJ-

For more information go to the following website: http://www.newbornscreening.info

PARENT FACT SHEET

DISORDER

Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)

CAUSE

MCAD occurs when an enzyme called "medium chain acyl-CoA dehydrogenase" is either missing or not working properly. This enzyme's job is to break down certain fats in the food we eat into energy. It also breaks down fat already stored in the body. Energy from fat keeps us going whenever our bodies run low of their main source of energy, a type of sugar called glucose. Our bodies rely on fat when we don't eat for a period of time.

IF NOT TREATED

When the MCAD enzyme is missing or not working, the body cannot use certain types of fat for energy and must rely solely on glucose. Although glucose is a good source of energy, there is a limited amount available. Once the glucose has been used up, the body tries to use fat without success. This leads to low blood sugar, called hypoglycemia, and to the build of harmful substances in the blood. This is called a metabolic crisis. Metabolic cri can cause permanent brain damage and even death.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed throughout life.

- Your child needs to avoid going a long time without food. This is to avoid a metabolic crisis. These childr should not go more than 4 to 6 hours without food and some may require more frequent feedings. It is important that these children be fed in the night – meaning you will need to wake them up to eat if they d not wake up on their own – and even if they are not hungry.
- Your metabolic specialist and dietician will design a low-fat, high carbohydrate diet for your child. This may include a special formula when your child is an infant. No changes in diet can happen without first getting permission from the metabolic specialist and dietician.
- Some children may benefit from taking L-carnitine. This is a safe and natural substance that helps the bo make energy. The metabolic specialist will decide if your child can benefit from this treatment. A prescription for this is required.
- Contact your child's doctor immediately at the start of any illness. Children with MCAD need to be treate in a hospital to prevent serious health problems.

IF TREATED

With prompt and careful treatment, children with MCAD usually live health lives with typical growth and development. The goal of treatment is to prevent long-term problems. However, children who have repeated metabolic crises may have life-long learning disabilities, uncontrolled movements in their muscles and tendons, o other effects.

Parent Fact Sheet

DISORDER

Methylmalonic Acidemia (Cbl A, B)

CAUSE

MMA stands for "methylmalonic acidemia". It is one type of organic acid disorder. People with MMA have problems breaking down and using certain amino acids and fatty acids from the food they eat.

IF NOT TREATED

MMA causes episodes of illness called metabolic crises. A metabolic crisis can cause harmful substances from the body to spill into the blood and urine.

If a metabolic crisis is not treated, a child with MMA can develop breathing problems, seizures, stroke and coma, sometimes leading to death. A metabolic crisis can be triggered by eating large amounts of protein, illness or infection, going too long without food, and stressful events such as surgery. Without treatment, brain and nerve damage can occur. This can cause mental retardation and problems with involuntary movements of the muscles and tendons. Death is common in untreated babies and children.

TREATMENT OPTIONS

- Your baby's primary doctor will work with a metabolic doctor and a dietician to care for your child. Prompt treatment is needed to reduce the chance for mental retardation and serious medical problems.
- Children with 'vitamin B12 responsive' MMA are given vitamin B12.
- Most children need to be on a low-protein diet and drink a special medical formula. You should start the treatments as soon as you know your child has MMA.
- Children who are having symptoms of a metabolic crisis should be treated in the hospital. During a metabolic crisis, your child may be given medications such as bicarbonate through an IV to help reduce the acid levels in the blood. Glucose is given by IV to prevent the breakdown of protein and fat stored in the body. Do not use any medication without checking with your doctor.
- A food plan low in the amino acids leucine, valine, methionine, and threonine with limited amounts of protein is often recommended. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Carbohydrates give the body many types of sugar that can be used as energy. Eating a diet high in carbohydrates and low in protein and fat can help prevent metabolic crises. Your dietician can create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. It is likely your child will need to be on a special food plan throughout life.
- Contact your child's doctor immediately at the start of any illness.

IF TREATED

Babies and children who have prompt and ongoing treatment may be able to live healthy lives with normal growth and development. In general, the earlier treatment is started, the better the outcome. Children who respond to vitamin B12 treatment tend to do very well as long as treatment is continued. Children who are not treated until after they have symptoms may have lasting health and learning problems. Even with treatment, some children develop life-long learning disabilities or mental retardation. In addition, despite treatment, seizures, involuntary movement disorders, and kidney failure have occurred in some children.

Parent Fact Sheet

DISORDER

Methylmalonic Acidemia Mutase Deficiency (MUT)

CAUSE

MMA stands for "methylmalonic acidemia". It is one type of organic acid disorder. People with MMA have problems breaking down and using certain amino acids and fatty acids from the food they eat.

IF NOT TREATED

MMA causes episodes of illness called metabolic crises. A metabolic crisis can cause harmful substances from the body to spill into the blood and urine. If a metabolic crisis is not treated, a child with MMA can develop breathing problems, seizures, stroke and coma, sometimes leading to death. A metabolic crisis can be triggered by eating large amounts of protein, illness or infection, going too long without food and stressful events such as surgery. Without treatment, brain and nerve damage can occur. This can cause mental retardation and problems with involuntary movements. Death is common in untreated babies and children.

TREATMENT OPTIONS

- Your baby's primary doctor will work with a metabolic doctor and a dietician to care for your child. Prompt treatment is needed to reduce the chance for mental retardation and serious medical problems. Children with 'vitamin B12 responsive' MMA are given vitamin B12. In addition, most children need to be on a low-protein diet and drink a special medical formula. You should start the treatments as soon as you know your child has MMA.
- Children who are having symptoms of a metabolic crisis should be treated in the hospital. During a metabolic crisis, your child may be given medications such as bicarbonate through an IV to help reduce the acid levels in the blood. Glucose is given by IV to prevent the breakdown of protein and fat stored in the body. Do not use any medication without checking with your doctor.
- A food plan low in the amino acids leucine, valine, methionine, and threonine with limited amounts of protein is often recommended. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Carbohydrates give the body many types of sugar that can be used as energy. Eating a diet high in carbohydrates and low in protein and fat can help prevent metabolic crises.
- Your dietician can create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. It is likely your child will need to be on a special food plan throughout life.

IF TREATED

Babies and children who have prompt and ongoing treatment may be able to live healthy lives with normal growth and development. In general, the earlier treatment is started, the better the outcome. Children who respond to vitamin B12 treatment tend to do very well as long as treatment is continued. Children who are not treated until after they have symptoms may have lasting health and learning problems. Even with treatment, some children develop life-long learning disabilities or mental retardation. In addition, despite treatment, seizures, involuntary movement disorders, and kidney failure have occurred in some children.

PARENT FACT SHEET

DISORDER

Multiple carboxylase deficiency (MCD)

CAUSE

MCD occurs when an enzyme called "holocarboxylase synthetase" (HCS) is either missing or not working properly. This enzyme's job is to add a vitamin called "biotin" to other enzymes called "carboxylases" so that they can change the food we eat into energy for the body. When the HCS enzyme is not working certain harmful substances build up in the blood and urine. This can cause serious health problems.

IF NOT TREATED

Each child with MCD is likely to have slightly different effects. Many babies with this condition start to have symptoms within hours of birth or during the first few days or weeks of life. Other babies have their first symptoms sometime in infancy, usually before two years of age. Without treatment, brain damage can occur. This can result in mental retardation or, sometimes, even death.

TREATMENT OPTIONS

Your child will need to be under the care of a metabolic specialist. Treatment is needed throughout life.

- The main treatment for MCD is a type of vitamin B called "biotin." In babies found to have MCD through newborn screening, biotin treatment can prevent symptoms from occurring. It can also reverse some of the health problems in children who have already shown symptoms.
- You will need a prescription from the metabolic specialist for biotin. They will determine the proper amount your child needs to take.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

Babies who receive prompt and ongoing treatment with biotin before they have a metabolic crisis are expected to have normal growth and development. Even with treatment, a few children have developed life-long learning problems or mental retardation. In children who have already show delays in learning, or a loss of hearing or eyesight, treatment can prevent additional effects. But it may not be able to correct the effects that are already present.

Parent Fact Sheet

DISORDER

Phenylketonuria (PKU)

CAUSE

PKU is one type of amino acid disorder. People with PKU have trouble breaking down an amino acid called phenylalanine from the food they eat. PKU occurs when an enzyme called "phenylalanine hydroxylase" is either missing or not working properly. This enzyme's job is to break down the amino acid phenylalanine. When a child with PKU eats foods with phenylalanine, it builds up in the blood and causes problems. It is found in almost every food, except pure fat and sugar.

IF NOT TREATED

The symptoms can vary from person to person. Babies with PKU seem perfectly normal at birth. The first effects are usually seen around 6 months of age. Untreated infants may be late learning to sit, crawl, and stand. They may pay less attention to things around them. Without treatment, a child with PKU will become mentally retarded.

Some of the effects of untreated PKU are: mental retardation, behavioral problems, hyperactivity, restlessness or irritability, seizures, eczema, musty or mousy body odor, fair hair and skin.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child. Lifelong treatment is usually needed.
- Prompt treatment is needed to prevent mental retardation. Newborns need to drink a special medical formula. It is possible to still breastfeed your baby as long as you get help from a dietician. Babies who are breastfed usually need the medical formula as well.
- A diet low in phenylalanine (Phe) is generally prescribed. Your child must not have cow's milk, regular formula, meat, fish, eggs or cheese. You must avoid the sugar substitute aspartame (Equal, NutraSweet) because it contains high levels of phenylalanine and can quickly raise the blood levels of Phe in people with PKU.
- Blood levels with have to be checked regularly to monitor the levels of PHE. The diet and formula may have to be adjusted.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

Children who receive early treatment and keep their Phe levels within the suggested ranges may be able to live healthy lives with typical growth and development. Some children may continue to have learning difficulties and other health problems despite treatment. If treatment is not started until 6 months of age, mental retardation often occurs. Treatment, even if started late, can help control behavior and mood problems and further prevent damage to the brain.

Parent Fact Sheet

DISORDER

Propionic Acidemia (PA)

CAUSE

Propionic Acidemia (PA) is one type of organic acid disorder. People with PA have problems breaking down and using certain amino acids from the foods they eat. PA occurs when an enzyme called "propionyl CoA carboxylase" is either missing or not working properly. When this enzyme is not working, substances called glycine and propionic acid along with other harmful substances build up in the blood and cause problems.

IF NOT TREATED

The symptoms can start as early as the first week of life. If untreated, harmful substances from the body spill into the blood and urine. This is called a metabolic acidosis. If a metabolic crisis is not treated, a child with PA can develop breathing problems, stroke, swelling of the brain, seizures and coma - sometimes leading to death.

A metabolic crisis can be triggered by eating large amounts of protein, illness or infection, going to long without food, and stressful events such as surgery.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child. Lifelong treatment is usually needed.
- Avoid going a long time without food. These babies need to eat more often to avoid low blood sugar. They should not go without eating for more than 4-6 hours. Some babies will need to eat more often than this.
- A low protein diet is often recommended. Your dietician will help plan any diet changes.
- Medical formula and foods contain the correct amount of protein and nutrients needed to for normal growth and development. Your metabolic doctor will tell you what type of formula is best and how much to use.
- A medication that has been found to be beneficial is L-Carnitine. It is a safe and natural substance that helps the body create energy and rid the body of harmful wastes. Unless you are advised otherwise, use only L-Carnitine prescribed by your doctor. Some children may be prescribed Biotin supplements, which is a type of B vitamin.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

It is not known how effective treatment is in preventing problems. Children who are treated early may be able to live healthy lives with typical growth and development. Some children may continue to have seizures, mental retardation, involuntary movements and other health problems despite treatment.

Parent Fact Sheet

DISORDER

Short Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)

CAUSE

People with Short Chain Acyl-CoA Dehydrogenase (SCAD) deficiency have problems breaking down fat into energy for their body. Most babies with newborn screening results showing SCAD never have symptoms. It occurs when an enzyme called "short chain Acyl-CoA dehydrogenase" is either missing or not working properly. It also breaks down fat already stored in the body.

Energy from fat keeps us going whenever our bodies run out of the main source of energy glucose. Our bodies rely on fat when we do not eat for a stretch of time-like sleeping during the night or missing a meal. Some people with SCAD cannot break down fat for energy. However, most people with SCAD do not seem to have this problem and do not ever develop symptoms.

IF NOT TREATED

The symptoms can start as early as the first week of life. If untreated, harmful substances from the body spill into the blood and urine. This is called a metabolic crisis. If a metabolic crisis is not treated, a child with SCAD can develop breathing problems, seizures and coma - sometimes leading to death.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child. Lifelong treatment is usually needed.
- Avoid going a long time without food. These babies need to eat more often to avoid low blood sugar. They should not go without eating for more than 4-6 hours. Some babies will need to eat more often than this.
- A low fat, high carbohydrate diet is often recommended. Your dietician will help plan any diet changes.
- L-Carnitine and Riboflavin may be prescribed by your doctor. L-Carnitine is a safe and natural substance that helps the body create energy and rid the body of harmful wastes. Riboflavin is vitamin B2 and a few children have been helped by taking it.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

It is not known how effective treatment is in preventing problems. Children who are treated early may be able to live healthy lives with typical growth and development. Some children may continue to have learning delays, muscle weakness and other health problems despite treatment.

Parent Fact Sheet

DISORDER

Sickle Cell Disease (HB S/S)

CAUSE

Sickle cell disease is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin S, an abnormal type of hemoglobin.

People with sickle cell conditions make a different form of hemoglobin called hemoglobin S (S stands for sickle). Red blood cells containing mostly hemoglobin S do not live as long as normal red blood cells (normally about 16 days). They also become stiff, distorted in shape and have difficulty passing through the body's small blood vessels. When sickle-shaped cells block small blood vessels, less blood can reach that part of the body. Tissue that does not receive a normal blood flow eventually becomes damaged. This is what causes the complications of sickle cell disease.

IF NOT TREATED

Untreated newborns often develop septicemia, an infection of the blood, and die within a few weeks of birth.

The leading cause of death in children with sickle cell disease in the United States is infection. The most troublesome germ is pneumococcus.

TREATMENT OPTIONS

- Health maintenance for patients with sickle cell disease starts with early diagnosis, preferably in the newborn period and includes penicillin prophylaxis, vaccination against pneumococcus bacteria and folic acid supplementation.
- Treatment of complications often includes: antibiotics, pain management, intravenous fluids, blood transfusion and surgery.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

Treatment for the symptoms of sickle cell disease has improved over the years and many people with sickle cell disease are living longer.

PARENT FACT SHEET

DISORDER

Trifunctional Protein Deficiency (TFP)

CAUSE

People with trifunctional protein (TFP) deficiency have problems breaking down fat into energy for their body. TFP deficiency occurs when a group of enzymes, called "trifunctional protein" is either missing or not working properly. The job of TFP is to breakdown certain fats from the food we eat into energy. It also breaks down fat already stored in the body.

Energy from fat keeps us going whenever our bodies run out of the main source of energy glucose. Our bodies rely on fat when we do not eat for a stretch of time-like sleeping during the night or missing a meal. When TFP is missing or not working well, the body cannot use fats for energy. Once all the glucose is used up, the body tries to use fat without success. This leads to low blood sugar and to the buildup of harmful substances in the blood.

IF NOT TREATED

The symptoms can vary from person to person. Babies with early TFP deficiency have episodes of illness called metabolic crisis. If untreated, harmful substances from the body spill into the blood and urine. This is called a metabolic crisis. If a metabolic crisis is not treated, a child with TFP deficiency can develop breathing problems, seizures, and coma - sometimes leading to death.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child. Lifelong treatment is usually needed.
- Avoid going a long time without food. These babies need to eat more often to avoid low blood sugar. They should not go without eating for more than 4-6 hours. Some babies will need to eat more often than this.
- A low fat, high carbohydrate diet is often recommended. Your dietician will help plan any diet changes.
- Medium Chain Triglyceride oil (MCT) and L-Carnitine is often used as part of the food plan for people with TFP deficiency. This special oil has medium chain fatty acids that can be used in small amounts for energy. You dietician will tell you how to use this supplement. You will have to get a prescription from the doctor for MCT oil.
- Contact your child's doctor immediately at the start of any illness

IF TREATED

Babies with TFP who receive treatment may have a prolonged life expectancy than without treatment.

PARENT FACT SHEET

DISORDER

Tyrosinemia, type 1 (TYR I)

CAUSE

People with tyrosinemia 1 have problems breaking down an amino acid called tyrosine from the food they eat. In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them. Tyrosinemia 1 occurs when an enzyme called fumarylacetoactoacetase (FAH) is either missing or not working properly.

IF NOT TREATED

The symptoms can vary from person to person. Children with TYR 1 usually smell like cabbage. Babies usually will have symptoms within the first few months of life. Without prompt and careful treatment, babies with severe liver and kidney problems usually die.

TREATMENT OPTIONS

- Your doctor will work with a metabolic specialist and dietician to care for your child. Lifelong treatment is usually needed to prevent liver and kidney problems.
- A medication called nitisinone (Orfadin®) is used to prevent liver and kidney damage. Your child should take this medication as soon as possible. Nitisinone will increase the level of tyrosine in your child's blood.
- Also a low tyrosine and low phenylalanine diet is very important. Your baby will have to avoid cow's milk, regular formula, meats, eggs and cheeses. A special formula will be ordered for your baby so they will get those nutrients and protein they will need to keep their levels within a safe range.
- Your child will have regular visits to the doctor as well as regular blood tests to see if there should be any changes to the medication. Contact your child's doctor immediately at the start of any illness.
- Liver transplant may be an option to prevent liver cancer.

IF TREATED

Children who are treated early usually live healthy lives with typical growth and development. When treatment is started early, severe kidney and neurologic symptoms can be prevented. If treatment is not started right away, liver and kidney damage may occur. Delays in growth and development may also be present.

PARENT FACT SHEET

DISORDER

Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD)

CAUSE

AD occurs when the very long chain acyl-CoA dehydrogenase enzyme is missing or not working properly. This me's job is to break down certain fats from the food we eat into energy. It also breaks down fat already stored in tl /.

IF NOT TREATED

AD is variable and can cause mild effects in some people and more serious health problems in others. Symptoms ı : in infancy or not until adulthood. There are three forms of VLCAD: Early, Childhood, and Adult.

TREATMENT OPTIONS

child will need to be under the care of a metabolic specialist and dietician. Treatment is usually needed througho

- Your child needs to avoid going a long time without food. This is to prevent a rapid drop in blood sugar. These children should not go more than 4 to 6 hours without food and some may require more frequent feedings. It important that these children be fed in the night – meaning you will need to be wake them up to eat if they do wake up on their own – even if they are not hungry.
- Frequently, a low fat, high carbohydrate diet is recommended. Your dietician will help develop your child's foc plan and no changes should be made without first getting the approval of the metabolic specialist and the dietician.
- Medium Chain Triglyceride oil (MCT oil) is often used as part of the child's food plan. You will require a prescription from the metabolic specialist to get this. The specialist and the dietician will assist you in how to properly use MCT oil.
- Some children take L-carnitine. It is a safe and natural substance that helps the body make energy. The metal specialist will decide if your child can benefit from this treatment. A prescription for this is also required.
- Contact your child's doctor immediately at the start of any illness. Children with VLCAD need to be treated in hospital to prevent serious health problems.
- Avoid your child's prolonged exercise or exertion.

IF TREATED

re diagnosis through newborn screening was possible, the early form of VLCAD was fatal. Now, with immediate a oing treatment, many infants are surviving. With prompt and careful treatment, people with childhood and adult ıs of VLCAD can often live healthy lives with typical growth and development.

The American College of Medical Genetics evaluated conditions for inclusion in newborn screening and has made recommendations, the following pages are conditions that were considered but not included in the final recommendation.

To be included as a primary target condition in a newborn screening program, a condition should meet the following minimum criteria:

- It can be identified at a phase (24 to 48 hours after birth) at which it would not ordinarily be clinically detected;
- A test with appropriate sensitivity and specificity is available for it;
- There are demonstrated benefits of early detection, timely intervention and efficacious treatment of the condition being tested.

Disorders Considered by American College of Medical Genetics for Newborn Screening But Not on Current Panel

Condition	Code
2-Methyl 3-hydroxy butyric aciduria	2M3HBA
2-Methylbutyryl-CoA dehydrogenase deficiency	2MBG
3-Methylglutaconic aciduria	3MGA
Adenosine deaminase deficiency	ADA
Arginine: glycine amidinotransferase deficiency	AGAT
Argininemia	ARG
Benign Hyperphenylalaninemia	H-PHE
Biliary atresia	BIL
Carbamylphosphate synthetase deficiency	CPS
Carnitine palmitoyltransferase Ia deficiency (L)	CPT IA
Carnitine palmitoyltransferase Ib deficiency (M)	CPT IB
Carnitine palmitoyltransferase II deficiency	CPTII
Carnitine/acylcarnitine translocase deficiency	CACT
Citrullinemia type II	CIT II
Congenital Cytomegalovirus infection	CMV
Congenital disorder of glycosylation type Ib	CDG Ib
Congenital Toxoplasmosis	TOXO
Creatine transporter defect	CR TRANS
Defects of biopterin cofactor biosynthesis	BIOPT BS
Defects of biopterin cofactor regeneration	BIOPT REG
Diabetes mellitus, insulin dependent	IDDM
Dienoyl-CoA reductase deficiency	DE-RED
Duchenne and Becker Muscular Dystrophy	DMD
Fabry disease	FABRY
Familial hypercholesterolemia (heterozygote)	FHC
Fragile X	FX
Galactokinase deficiency	GALK
Galactose epimerase deficiency	GALE
Glucose-6-phosphate dehydrogenase deficiency	G6PD
Glutaric acidemia type II	GA2
Guanidinoacetate methyltransferase deficiency	GAMT
Human HIV infection	HIV
Hurler-Scheie disease	MPS-1H

Condition	Code
Hyperbilirubinemia*	HPRBIL
Hypermethioninemia	MET
Isobutyryl-CoA dehydrogenase deficiency	IBG
Krabbe disease	KRABBE
Lysosomal storage diseases	LSD
Malonic aciduria	MAL
Medium chain ketoacyl-CoA thiolase deficiency	MCKAT
Medium/short-chain 3-OH acyl-CoA DH def.	M/SCHAD
Methylmalonic acidemia (Cbl C,D)	Cbl C,D
Neuroblastoma	NB
Ornithine transcarbamylase deficiency	OTC
Other variant Hb-pathies (including Hb E)	Var Hb
Pompe disease	POMPE
Severe combined immunodeficiency	SCID
Smith-Lemli-Opitz syndrome	SLO
Turner syndrome	TURNER
Tyrosinemia type II	TYR II
Tyrosinemia type III	TYR III
Wilson disease	WD
X-linked Adrenoleukodystrophy	ALD
α1-Antitrypsin deficiency	α1AT

Index to Diseases

Condition	Code	Page #
Diabetes mellitus, insulin dependent	IDDM	10B
Dienoyl-CoA reductase deficiency	DE-RED	10B
Duchenne and Becker Muscular Dystrophy	DMD	10B
Fabry disease	FABRY	10B
Familial hypercholesterolemia (heterozygote)	FHC	10B
Fragile X	FX	10B
Galactokinase deficiency	GALK	10B
Galactosemia (Classic)	GALT	8S-8T
Galactose epimerase deficiency	GALE	10B
Glucose-6-phosphate dehydrogenase deficiency	G6PD	10B
Glutaric acidemia type I	GA I	8U-8V
Glutaric acidemia type II	GA2	10B
Guanidinoacetate methyltransferase deficiency	GAMT	10B
Hearing loss	HEAR	6E
Hemoglobin S/β-thalassemia	Hb S/ßThal	8W-8X
Hemoglobin S/C disease	Hb S/C	8Y-8Z
Hemoglobin SS disease (Sickle cell anemia)	Hb SS	8AY-8AZ
Homocystinuria	HCY	8AA-8AB
Human HIV infection	HIV	10B
Hurler-Scheie disease	MPS-1H	10B
Hydroxymethylglutaric aciduria	HMG	8AC-8AD
Hyperbilirubinemia	HPRBIL	10B
Hypermethioninemia	MET	10C
Isobutyryl-CoA dehydrogenase deficiency	IBG	10C
Isovaleric acidemia	IVA	8AE-8AF
Krabbe disease	KRABBE	10C
Long-chain 3-OH acyl-CoA dehydrogenase def.	LCHAD	8AG-8AH
Lysosomal storage diseases	LSD	10C
Malonic aciduria	MAL	10C
Maple syrup (urine) disease	MSUD	9AI-8AJ
Medium chain ketoacyl-CoA thiolase deficiency	MCKAT	10C
Medium/short-chain 3-OH acyl-CoA DH def.	M/SCHAD	10C
Medium-chain acyl-CoA dehydrogenase deficiency	MCAD	8AK-8AL
Methylmalonic acidemia (Cbl A, B)	Cbl A,B	8AM-8AN

Condition	Code	Page #
Methylmalonic acidemia (Cbl C,D)	Cbl C,D	10C
Methylmalonic acidemia (mutase)	MUT	8AO-8AP
Multiple carboxylase deficiency	MCD	8AQ-8AR
Neuroblastoma	NB	10C
Ornithine transcarbamylase deficiency	OTC	10C
Other variant Hb-pathies (including Hb E)	Var Hb	10C
Phenylketonuria	PKU	8AS-8AT
Pompe disease	POMPE	10C
Propionic acidemia	PA	8AU-8AV
Severe combined immunodeficiency	SCID	10C
Short-chain acyl-CoA dehydrogenase deficiency	SCAD	8AW-8AX
Sickle cell anemia (Hemoglobin SS disease)	Hb SS	8AY-8AZ
Smith-Lemli-Opitz syndrome	SLO	10C
Trifunctional protein deficiency	TFP	8BA-8BB
Turner syndrome	TURNER	10C
Tyrosinemia type I	TYR I	8BC-8BD
Tyrosinemia type II	TYR II	10C
Tyrosinemia type III	TYR III	10C
Very long-chain acyl-CoA dehydrogenase def.	VLCAD	8BE-8BF
Wilson disease	WD	10C
X-linked Adrenoleukodystrophy	ALD	10C
α1-Antitrypsin deficiency	α1AT	10C
β-Ketothiolase deficiency	βKT	8E-8F